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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
REGION III
1650 Arch Street
Philadelphia, Pennsylvania 19103-2029

March 14, 2002

Ms. Lydia Guy
Regional Hearing Clerk (3RC00)
U.S. EPA, Region III
1650 Arch Street
Philadelphia, PA 19103-2029

Re: E.I. du Pont de Nemours and Company, Incorporated
EPA Docket Nos. SDWA-03-2002-0019; SDWA-05-2002-0002

Dear Ms. Guy:

Please find enclosed for filing an original copy of the order on consent in the above-captioned matter, copies of which were filed with you on March 11, 2002.

Sincerely,

Janet E. Sharke
Sr. Asst. Regional Counsel

cc: Bernard J. Reilly, Esq.
Paul Bossert, Jr.

DOCUMENT 50

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

REGION III
1650 ARCH STREET
PHILADELPHIA, PA 19103

REGION V
77 WEST JACKSON BOULEVARD
CHICAGO, IL 60604

IN THE MATTER OF:	)	
	)	ORDER ON CONSENT
	)	
E. I. du Pont de Nemours	)	
and Company, Incorporated	)	Proceeding under section 1431(a)(1)
	)	of the Safe Drinking Water Act,
	)	42 U.S.C. § 300i(a)(1)
Washington Works Facility	)	
Route 892	)	Docket Nos. SDWA-03-2002-0019,
Washington, WV 26181	)	SDWA-05-2002-0002

I. STATUTORY AUTHORITY

1. This Order on Consent ("Order") is issued pursuant to the authority vested in the Administrator of the United States Environmental Protection Agency ("EPA") by Section 1431(a)(1) of the Safe Drinking Water Act ("SDWA"), 42 U.S.C. § 300i(a)(1).

2. The authority to issue this Order was delegated to the Regional Administrators by Delegation No. 9-17, dated May 11, 1994.

3. Under the SDWA, Congress has delegated to EPA broad authority for the protection of public water supplies and drinking water sources.

II. DEFINITIONS

4. The term "Underground Source of Drinking Water" ("USDW") means an "aquifer" or its portion which supplies a public water system ("PWS") or which contains a sufficient quantity of ground water to supply a PWS and which currently supplies drinking water for human consumption, or contains fewer than 10,000 milligrams per liter (mg/l) total dissolved solids, and is not an exempted aquifer. See 40 C.F.R. § 144.3.

III. FINDINGS OF FACT AND CONCLUSIONS OF LAW

5. E. I. du Pont de Nemours and Company, Incorporated ("DuPont"), is a corporation and is therefore a "person" within the meaning of Section 1401(12) of the SDWA, 42 U.S.C. § 300f(12).

6. DuPont owns and operates a manufacturing facility, known as the Washington Works ("Facility"), located in Washington, Wood County, West Virginia.

7. Ammonium perfluorooctanoate, CAS Number 3825-26-1 (hereafter "C-8"), is a perfluorinated surfactant that DuPont has used in its fluoropolymer-related manufacturing processes at the Facility since the early 1950s.

8. Residues containing C-8 generated by the Facility are or have been released to the air, discharged to the Ohio River, disposed of at the Facility, Dry Run and Letart landfills in West Virginia ("disposal sites") and otherwise shipped off-site for destruction and/or disposal including into unlined landfills.

9. Studies performed by DuPont and Minnesota Manufacturing and Mining Corporation (a manufacturer of C-8) ("3M") have determined that C-8 in sufficient doses, i.e., considering both amount and duration of exposure, is toxic to animals through ingestion, inhalation and dermal contact. Studies have also found that C-8 is persistent in humans and the environment. EPA is conducting a preliminary hazard assessment of C-8 under the Toxic Substances Control Act ("TSCA").

10. Recently, C-8 has been detected in the underground source of drinking water used to supply the following locations, at the following levels :

Lubeck, WV, PSD:	0.8 micrograms/liter (ug/l) (1st quarter 2000)
Facility Production Wells:	1.99 ug/l (Well 336, 1998) 1.45 ug/l (Well 332, 1999)
Facility Drinking Water Taps:	0.213 ug/l (Building 5, 1999) 0.496 ug/l (Building 293, 1999) 0.306 ug/l (Building 231, 1999) 0.135 ug/l (Building 363, 2000)
Little Hocking, OH, PWS:	1.840 ug/l (Well 1, 12/01) 3.730 ug/l (Well 2, 12/01) 0.855 ug/l (Well 3, 12/01) 7.690 ug/l (Well 5, 12/01) 1.720 ug/l (Well 1, 1/02) 2.970 ug/l (Well 2, 1/02) 0.744 ug/l (Well 3, 1/02)

6.220 ug/l (Well 5, 1/02)

11. Although recent sampling shows lower levels, groundwater data from Letart landfill has shown C-8 concentrations as high as:

On-site monitoring well MW1	24,000 ug/l (1998)
On-site monitoring well MW-2A	990 ug/l (1998)

Private wells near the Letart landfill when tested for C-8 in 2001 showed levels of 0.42 ug/l, 0.296 ug/l, and 0.085 ug/l; tap samples from the only well in the area of Letart landfill which is currently known to supply drinking water showed levels of 0.031 ug/l, 0.046 ug/l and 0.053 ug/l (duplicate sample).

12. The C-8 discharged by the Facility is a contaminant present in or is likely to enter a PWS or an USDW through the migration from air emissions, surface water discharges or from unlined landfills, and may present an imminent and substantial endangerment at levels exceeding 14 ug/l in water used for human consumption based on "A Hazard Narrative for Perfluorooctanoate (PFOA)" a final report prepared by ENVIRON International Corporation, January 24, 2002 (hereafter "ENVIRON report") for DuPont.

13. DuPont, the West Virginia Department of Environmental Protection("WVDEP"), and the West Virginia Department of Health and Human Resources ("WVDHHR") have entered in an agreement on consent ("WV Order"), dated November 15, 2001, attached hereto, which provides for, *inter alia*, a toxicological and human health risk assessment of C-8 to be conducted under the supervision of a C-8 Assessment of Toxicity ("CAT") Team pursuant to the WV Order, as well as ground and surface water monitoring and plume identification. DuPont, in a letter dated February 11, 2002, attached hereto, also agreed to perform sampling of private and public ground water wells within a 1-mile radius of the Little Hocking, Ohio PWS well field, following the protocol established in the WV Order. (Hereafter, the sampling required by the WV Order and the additional sampling agreed to by DuPont will be referred to as "sampling in WV/OH.")

14. C-8 is currently not a contaminant for which a national primary drinking water regulation has been established pursuant to the SDWA, however, for the purpose of this Order, DuPont and EPA agree to use the level of 14 ug/l C-8, as set forth in the ENVIRON report, as the temporary threshold level for provision of alternate water as required by paragraph 17 of this Order.

15. DuPont and EPA further agree to use the screening level for C-8 to be established by the WV Order as the threshold level for the provision of alternate water required by paragraphs 18 through 23 of this Order, in lieu of the level set forth in paragraphs 12 and 14 of this Order.

16. EPA has consulted with the WVDEP, WVDHHR, the Ohio Environmental Protection Agency ("OEPA") and the Ohio Department of Health ("ODH") to confirm that the information on which this Order is based is correct and to ascertain the action that the state and local authorities are or will be taking. WVDHHR, OEPA, and ODH have requested that EPA take this action. EPA has concluded that all requisite conditions have been satisfied for EPA action under Section 1431(a)(1) of the SDWA, 42 U.S.C. § 300i(a)(1).

IV. ORDER ON CONSENT

Pursuant to the authority issued to the EPA Administrator by Section 1431(a)(1) of the SDWA, 42 U.S.C. § 300i(a)(1), and delegated to the Regional Administrators, DuPont is ORDERED and hereby consents to the following:

Provision of Alternate Drinking Water

17. As soon as practicable, but not later than fifteen (15) days following receipt of validated sampling results performed in accordance with the WV Order for sampling in WV/ OH, DuPont shall provide a temporary alternate drinking water supply for users of any private drinking water well and PWS in West Virginia or Ohio where such results show the level of C-8 exceeds 14 ug/l. A "temporary alternate drinking water supply" shall mean connection to a PWS, connection to a new water well, adequately treated water or water from some other source, including bottled water or bulk water from a tank truck that meets the water quality requirements of 40 C.F.R. § 141 and has a level of C-8 no greater than 14 ug/l; is in sufficient quantity for all reasonable domestic uses including drinking and cooking; and is provided in a manner convenient to the users. DuPont shall continue to provide this temporary alternate drinking water supply until DuPont fully implements the Alternate Drinking Water Plan pursuant to paragraphs 18 through 23 of this Order. DuPont shall be responsible for all operation and maintenance costs of the alternate drinking water supply.

18. As soon as practicable but not later than thirty (30) days after a determination by the Groundwater Investigation Steering Team ("GIST") established pursuant to the WV Order that a private drinking water well or PWS in West Virginia or Ohio contains C-8 at levels greater than the screening level developed pursuant to the WV Order, DuPont shall submit to EPA for approval, and to WVDHHR, WVDEP and OEPA, as appropriate, for review, an Alternate Drinking Water Plan which identifies all actions necessary to enable DuPont to fully comply with the requirements of paragraph19 through 23 of this Order. The Alternate Drinking Water Plan shall include a schedule of implementation for such actions.

19. The Alternate Drinking Water Plan shall provide that:

a. DuPont shall assure the provision of an alternate supply of drinking water to all users of any PWS and any private drinking water well in West Virginia or Ohio, identified pursuant to sampling in WV/OH, where, and for so long as, the level of C-8 exceeds the screening level developed pursuant to the WV Order.

b. Such levels shall be determined by monitoring performed using a test procedure established by the GIST pursuant to the WV Order. Such alternate supply of drinking water is to be provided at no cost to the users of such PWS or private drinking water wells, except for usual service fees incurred by users of a PWS.

c. DuPont will provide notice to all users of such PWS and private drinking water wells of the availability of the alternate supply of drinking water.

d. An "alternate supply of drinking water" shall mean connection to a PWS, connection to new water well, adequately treated water or water from some other source, acceptable to EPA, that meets the water quality requirements of 40 C.F.R. § 141 and has a level of C-8 no greater than the screening level established pursuant to the WV Order; is in sufficient quantity for all reasonable domestic uses including drinking and cooking; and is provided in a manner convenient to the users. DuPont shall be responsible for all operation and maintenance costs of the alternate supply of drinking water for the duration of operation pursuant to this Order, unless the alternate supply of drinking water is provided by connection to a PWS.

20. Following the initial submittal of the Alternate Drinking Water Plan by DuPont, if EPA, in consultation with WVDHHR, WVDEP, and OEPA, as appropriate, determines that modifications are necessary to DuPont's Alternate Drinking Water Plan, DuPont shall make such modifications as EPA may specify to satisfy the requirements of this Order and submit a revised Alternate Drinking Water Plan within forty-five (45) calendar days of notification by EPA.

21. Upon EPA's approval of the Alternate Drinking Water Plan (or revised Alternate Drinking Water Plan, as the case may be), DuPont shall implement, in accordance with the approved schedule, any and all actions necessary to comply with the requirements of paragraphs 18-20.

22. Within thirty (30) calendar days of EPA's approval of the Alternate Drinking Water Plan (or revised Alternate Drinking Water Plan, as the case may be), and quarterly thereafter, DuPont shall submit to EPA, WVDHHR, WVDEP, and OEPA, written reports summarizing all actions taken in accordance with this Order ("progress reports"). DuPont shall continue to submit progress reports until such time as EPA provides written notice that the reports are no longer necessary, or this Order is terminated.

All progress reports required by this paragraph shall contain the following certification, which shall be signed by a responsible corporate officer:

> I certify under penalty of law that this document and all attachments were prepared under my direction or supervision in accordance with a system designed to assure that qualified personnel properly gathered and evaluated the information submitted. Based on my inquiry of the person or persons who manage the system, or those persons directly responsible for gathering the information, the information submitted is, to the best of my knowledge and belief, true, accurate, and complete. I am aware that there are significant penalties for submitting false information, including the possibility of fines and imprisonment for knowing violations.

For purposes of this Order, a responsible corporate officer shall be (i) a president, secretary, treasurer, or vice-president of DuPont in charge of a principal business function, or any other person who performs similar policy- or decision-making functions for DuPont, or (ii) the manager of the Facility, if the Facility employs more than 250 persons or has gross annual sales or

expenditures exceeding $25 million (in second quarter 1980 dollars), if authority to sign documents has been delegated to the manager in accordance with corporate procedures.

23. All submittals, including reports, required under this Order shall be submitted to the following addressees:

As to EPA:

Roger Reinhart (3WP32)
U.S. EPA Region III
1650 Arch Street
Philadelphia, PA 19103-2029

Kelley Moore (WG-15J)
U.S. EPA Region V
77 West Jackson Boulevard
Chicago, IL 60604

As to WVDHHR:

Victor Wilford
Division of Environmental Engineering
Office of Environmental Health Services
Department of Health and Human Resources
815 Quarrier Street, Suite 418
Charleston, WV 25301

As to WVDEP:

David Watkins
Ground Water Protection Section
Division of Water Resources
West Virginia Department of Environmental Protection
1201 Greenbrier Street
Charleston WV 25301

As to OEPA:

Michael Baker
Division of Drinking & Ground Waters
Ohio Environmental Protection Agency
122 South Front Street
Columbus, OH 43215

V. GENERAL PROVISIONS

24. DuPont admits the jurisdictional allegations set forth herein and waives any defenses it might have as to jurisdiction and venue and agrees not to contest any of the findings of fact or conclusions of law herein in any action to enforce this Order. Except as to any proceeding brought by EPA to enforce this Order, in agreeing to this Order DuPont makes no admission of fact or law and reserves all rights and defenses available regarding liability or responsibility in any other legal proceeding related to the subject matter of this Order.

25. This Order shall apply to and be binding upon DuPont and its agents, successors, and assigns.

26. This Order may be modified only upon written consent of all parties.

27. Nothing in this Order shall be construed as prohibiting, altering or in any way eliminating the ability of EPA to seek any other remedies or sanctions available by virtue of DuPont's violations of this Order or of the statutes and regulations upon which this Order is based or for DuPont's violation of any applicable provision of law.

28. This Order shall not relieve DuPont of its obligation to comply with all applicable provisions of federal, state or local law, nor shall it be construed to be a ruling on, or determination of, any issue related to any federal, state or local permit.

29. Nothing in this Order is intended to nor shall be construed to operate in any way to resolve any criminal liability of DuPont. Compliance with this Order shall not be a defense to any actions subsequently commenced for any violation of federal laws and regulations administered by EPA, and it is the responsibility of DuPont to comply with such laws and regulations. EPA reserves the right to undertake action against any person, including DuPont, in response to any condition which EPA determines may present an imminent and substantial endangerment to the public health, public welfare or the environment.

30. The undersigned representative of DuPont certifies that he is fully authorized by DuPont to enter into the terms and conditions of this Order and to execute and legally bind that party to it.

31. Pursuant to Section 1431(b) of the SDWA, 42 U.S.C. § 300i(b), violation of any term of this Order, or failure or refusal to comply with this Order, may subject DuPont to a civil penalty of up to $15,000 per day per violation for each such day in which a violation occurs or failure to comply continues, as assessed by an appropriate United States District Court.

32. When DuPont knows or should have known, by the exercise of due diligence, of an event that might delay completion of any requirement of this Order, DuPont shall provide notice to EPA, in writing, within ten (10) business days after DuPont first knew, or in the exercise of due diligence, should have known, of such event. The notice shall describe in detail the basis for the delay, including whether it is a Force Majeure event, and describe the length of, precise cause(s) of, and measures to be taken to prevent or minimize such delay. If EPA agrees that such event constitutes Force Majeure, EPA shall extend the time for performance of such requirement, in

writing, to compensate for the delay caused by the Force Majeure event. DuPont's failure to notify EPA in accordance with this paragraph shall render this paragraph void and of no effect. For purposes of this Order, Force Majeure is defined as an event arising from the causes beyond the control of DuPont, and any entity controlled by DuPont, which delays or prevents the performance of any obligation under this Order. Unanticipated or increased costs or expenses associated with the implementation of this Order and changed financial circumstances, failure to apply for a required permit or approval or to provide in a timely manner all information to obtain a permit or approval or to obtain or approve contracts, shall not, in any event, constitute Force Majeure events. DuPont reserves what ever rights it may have to dispute EPA's determination that a particular event does not constitute Force Majeure in any action to enforce this Order.

33. This Order shall be effective upon execution by all parties. This Order shall remain in effect until DuPont fulfills its obligations pursuant to paragraphs 17 through 23 herein, submits a written request to EPA to terminate this Order, and EPA approves such termination request.

34. This Consent Order may be executed in any number of counterpart originals, each of which shall be deemed to constitute an original agreement, and all of which shall constitute one agreement. The execution of one counterpart by any party shall have the same force and effect as if that party had signed all other counterparts.

35. All of the terms and conditions of this Order together comprise one agreement, and each of the terms and conditions is in consideration of all of the other terms and conditions. In the event that this Order, or one or more of its terms and conditions, is held invalid, or is not executed by all of the signatories in identical form, or is not approved in such identical form by the Regional Administrators, then the entire Order shall be null and void.

SO ORDERED:

_____ Date: _____

Donald S. Welsh
Regional Administrator
U.S. Environmental Protection Agency, Region III

_____ Date: 3.7.02

Thomas V. Skinner
Regional Administrator
U.S. Environmental Protection Agency, Region V

writing, to compensate for the delay caused by the Force Majeure event. DuPont's failure to notify EPA in accordance with this paragraph shall render this paragraph void and of no effect. For purposes of this Order, Force Majeure is defined as an event arising from the causes beyond the control of DuPont, and any entity controlled by DuPont, which delays or prevents the performance of any obligation under this Order. Unanticipated or increased costs or expenses associated with the implementation of this Order and changed financial circumstances, failure to apply for a required permit or approval or to provide in a timely manner all information to obtain a permit or approval or to obtain or approve contracts, shall not, in any event, constitute Force Majeure events. DuPont reserves what ever rights it may have to dispute EPA's determination that a particular event does not constitute Force Majeure in any action to enforce this Order.

33. This Order shall be effective upon execution by all parties. This Order shall remain in effect until DuPont fulfills its obligations pursuant to paragraphs 17 through 23 herein, submits a written request to EPA to terminate this Order, and EPA approves such termination request.

34. This Consent Order may be executed in any number of counterpart originals, each of which shall be deemed to constitute an original agreement, and all of which shall constitute one agreement. The execution of one counterpart by any party shall have the same force and effect as if that party had signed all other counterparts.

35. All of the terms and conditions of this Order together comprise one agreement, and each of the terms and conditions is in consideration of all of the other terms and conditions. In the event that this Order, or one or more of its terms and conditions, is held invalid, or is not executed by all of the signatories in identical form, or is not approved in such identical form by the Regional Administrators, then the entire Order shall be null and void.

SO ORDERED:

Donald S. Welsh

MAR 7 2002

Date: _____

Donald S. Welsh
Regional Administrator
U.S. Environmental Protection Agency, Region III

_____

Date: _____

Thomas V. Skinner
Regional Administrator
U.S. Environmental Protection Agency, Region V

AGREED TO:

Paul J. Bossert, Jr Date: March 4, 2002

Paul Bossert
Plant Manager, Washington Works Facility
E. I. du Pont de Nemours and Company, Incorporated

CONSENT ORDER ISSUED PURSUANT TO ARTICLES 5 and 12, CHAPTER 22 AND ARTICLE 1, CHAPTER 16 OF THE WEST VIRGINIA CODE.

TO: E. I. DU PONT DE NEMOURS AND COMPANY DATE: November 14, 2001

West Virginia Department of Environmental Protection **Order No. GWR-2001-019**
West Virginia Department of Health and Human Resources

This **CONSENT ORDER** is issued by the Director of the Division of Water Resources and Director of the Division of Air Quality, West Virginia Department of Environmental Protection, and the Commissioner of the Bureau for Public Health, West Virginia Department of Health and Human Resources, pursuant to the authority set forth in more detail below.

I. INTRODUCTION OF PARTIES.

This Consent Order is entered into by and between the West Virginia Department of Environmental Protection [WVDEP], the West Virginia Department of Health and Human Resources – Bureau for Public Health [WVDHHR-BPH], and E. I. du Pont de Nemours and Company [DuPont][collectively referred to as the "Parties"].

II. PURPOSE OF CONSENT ORDER.

This Consent Order sets forth a series of tasks to be performed by the Parties in order to determine whether there has been any impact on human health and the environment as a result of releases of ammonium perfluorooctanoate [C8], CAS Number 3825-26-1, to the environment from DuPont operations. C8 is a material used by DuPont in its fluoroproducts manufacturing process at its Washington Works facility located at Washington, Wood County, West Virginia. C8 is not identified as a hazardous substance, hazardous waste or otherwise specifically regulated under West Virginia or federal statute or regulation.

This Consent Order has been negotiated in good faith and the actions undertaken by DuPont pursuant to this Consent Order do not constitute an admission of any liability on its part. DuPont retains the right to controvert in any other proceedings, other than proceedings to implement or enforce this Consent Order, the validity of the findings of fact and conclusions of law set forth herein. DuPont agrees to comply with and be bound by the terms of this Consent Order and further agrees in any proceeding to implement or enforce this Consent Order that it

will not contest the validity of this Consent Order or the jurisdiction of WVDEP and WVDHHR-BPH to issue it.

III. DEFINITIONS.

Whenever the terms identified below are used in the Consent Order or in any exhibit or attachment hereto, the following definitions shall apply:

1. "The Agencies" shall mean the Department of Health and Human Resources, Bureau for Public Health and the Department of Environmental Protection, including the Divisions of Air Quality and Water Resources.

2. "C8" shall mean the chemical compound ammonium perfluorooctanoate.

3. "Detection Limit" means the lowest analytical level that can be reliably achieved within specified limits of precision and accuracy under routine laboratory conditions for a specified matrix. It is based on quantitation, precision and accuracy under normal operation of a laboratory and the practical need in a compliance-monitoring program to have a sufficient number of laboratories available to conduct the analyses.

4. "Effective Date" shall mean the date set forth in Section XVII of this Consent Order.

5. "EPA" shall mean the United States Environmental Protection Agency.

6. "Force Majeure" shall mean conditions or circumstances beyond the reasonable control of DuPont which could not have been overcome by due diligence and shall include, without limitation, acts of God, action or inaction of governmental agencies, or administrative or judicial tribunals or other third parties, or strikes or labor disputes (provided, however, DuPont shall not be required to concede to any labor demands), which prevent or delay DuPont from complying with the work plan.

7. "Groundwater Monitoring Well" shall mean any cased excavation or opening into the ground made by digging, boring, drilling, driving, jetting, or other methods for the purpose of determining the physical, chemical, biological, or radiological properties of groundwater. The term "monitoring well" includes piezometers and observation wells, which are installed for purposes other than those listed above, but does not include wells whose primary purpose is to provide a supply of potable water.

8. "Groundwater Well" or "Well" shall mean any drilled or excavated groundwater collection system that supplies water for public, private, industrial, or agricultural use and shall include drinking water wells. As used in this Consent Order, this term applies only to wells

located in West Virginia.

9. "Reimbursable Costs" shall mean costs attributable (on an hourly basis) to the work of Dee Ann Staats, Ph.D. in the negotiation and implementation of this Consent Order, the costs attributable to any other participants on the C8 Assessment of Toxicity Team, as described in Attachment C to this Consent Order, who are serving in that position as contractors to WVDEP, costs incurred by WVDEP in connection with the public meetings described in Attachment C, and costs attributable to any contractor retained at the direction of the Groundwater Investigation Steering Team (GIST).

10. "Washington Works" shall mean the manufacturing facility owned by DuPont and located in Washington, Wood County, West Virginia, as depicted on Exhibit 1 to this Consent Order.

11. "The Facilities" shall mean the Washington Works and the Local Landfill, depicted on Exhibit 1, the Letart Landfill, depicted on Exhibit 2, and the Dry Run Landfill, depicted on Exhibit 3.

12. "Reference Dose" or "RfD" shall mean an estimate (with uncertainty spanning perhaps an order of magnitude or greater) of a daily exposure level for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects during a lifetime. Chronic RfDs are specifically developed to be protective for long-term exposure to a compound.

13. "Screening Level" shall mean the concentration in a specific media such as air, water, or soil, that is likely to be without an appreciable risk of deleterious effects during a lifetime in the human population.

IV. WAIVER OF RIGHTS.

DuPont waives any and all rights it may have to appeal or challenge the validity or requirements of this Consent Order, and shall not challenge the jurisdiction of the Agencies to issue this Consent Order.

This Consent Order applies to and is binding upon the Parties, and their successors and assigns.

V. FINDINGS OF FACT.

1. C8 is a chemical substance which has no established state or federal effluent or emission standards.

2. C8 is a perfluorinated surfactant manufactured by the 3M Company and others.

Since the early 1950's C8 has been used by DuPont in its fluoropolymer-related manufacturing processes at its Washington Works facility, located in Wood County, West Virginia.

3. Residues containing C8 from fluoropolymer manufacturing processes at Washington Works are or have been released to the air, discharged to the Ohio River, disposed of at the Facilities, and otherwise shipped off-site for destruction and/or disposal. DuPont also captures for recycle a significant portion of used C8.

4. No permits issued to DuPont authorizing releases of pollutants to the environment contain specific limitations on the amount of C8 that may be released to the environment. However, C8 releases are addressed more generally in WVDEP Division of Air Quality permits as particulate matter, PM_{10} (particulate matter with an aerodynamic diameter less than or equal to 10 microns), or as a volatile organic compound.

5. Since as early as 1990, DuPont has performed regular, voluntary water sampling to detect the presence and level of C8 in and around certain of its Facilities in West Virginia and has reported the results of this sampling to various government agencies. Currently, DuPont also samples and reports C8 concentrations in water as required by permits issued by WVDEP and EPA.

6. As a result of DuPont's sampling, C8 has been detected in varying concentrations in and around certain of its Facilities in West Virginia, including private drinking water wells and public water supplies.

7. Analyses of water samples have reported levels of C8 in the Lubeck Public Service District ("LPSD") drinking water supply.

8. DuPont, by and through its use of C8 in the fluoropolymer manufacturing process, is the likely source of C8 presence in and around certain of its Facilities in West Virginia.

9. Along with environmental sampling for C8, DuPont has performed and participated in multiple studies examining the potential effects of C8 exposure on human health and the environment.

10. Studies performed by DuPont and 3M have determined that C8 in sufficient doses, i.e., considering both amount and duration of exposure, is toxic to animals through ingestion, inhalation and dermal contact. Studies have also found that C8 is persistent in humans and the environment.

11. Although DuPont has collected a large amount of data on the presence of C8 in the environment, the Agencies believe that additional information will assist them in delineating the extent and concentrations of C8 in the environment at or near the Facilities. Available data collected by DuPont indicates that C8 is present in the surface and groundwater at the Letart and

Dry Run Landfills and at or near the Washington Works facility.

12. WVDEP and WVDHHR-BPH have determined that it is desirable to ascertain the source of drinking water for persons potentially exposed to C8 in groundwater or surface waters in the area of the Facilities.

13. EPA, WVDEP, and WVDHHR-BPH, in consultation and cooperation with one another, have requested, and DuPont has submitted, information and documents relating to the detection and presence of C8 in and around the Facilities and documents with respect to the human health studies being performed related to C8 exposure.

14. Based upon information submitted by DuPont and reviewed to date by EPA, WVDEP, and WVDHHR-BPH, the Agencies believe that additional data would assist in their evaluation of whether the ground and surface waters now containing C8 have a complete exposure pathway to humans and whether persons in and around the Facilities are at risk of adverse health effects from C8 exposure.

15. There have been no independent governmental or non-industrial studies performed on the human health effects of C8 exposure for the purpose of establishing an exposure standard for C8 applicable to the general public.

16. The Agencies have concluded that full site and health assessments are necessary to ascertain the extent and level of C8 concentrations in the environment and to assist them in determining whether C8 presents any possible danger to the public. DuPont has agreed to participate and assist in this effort.

17. The fluoropolymers industry has committed to EPA to reduce total actual C8 emissions for either the year 1999 or the year 2000 by 50 percent within three to five years of each company's commitment date. DuPont committed to this goal in 2000.

18. DuPont installed, in March 2001, a filter and carbon treatment system at its Washington Works facility that is demonstrating removal efficiency of 90-95% of the C8 in its major C8-containing wastewater stream.

VI. AUTHORITY TO ISSUE CONSENT ORDER.

1. The WVDEP is the state agency vested with the authority to protect the environment in West Virginia.

2. Article 12, Chapter 22 of the West Virginia Code, the Groundwater Protection Act, grants to the WVDEP the authority to protect the State's groundwater from any contaminant

and, where contaminated groundwater is found, to institute a civil action or issue an order requiring that groundwater be remediated.

3. Article 5, Chapter 22 of the West Virginia Code, the Air Pollution Control Act, grants to the WVDEP the authority to protect the State's air from pollutants and to institute a civil action or issue orders to enforce the statute.

4. The WVDHHR-BPH is the state agency vested with the authority to regulate and protect drinking water supplies in West Virginia.

5. Article 1, Chapter 16 of the West Virginia Code, grants to the WVDHHR-BPH the authority to protect the public drinking water supply of the state and to perform all investigation necessary to assure its purity and safety, and further grants to the WVDHHR-BPH the authority to institute actions and issue orders to restore the purity of said water supply.

VII. REQUIREMENTS OF CONSENT ORDER.

The Agencies have concluded that it is of great importance to have sufficient data upon which to determine the scope and potential risk of the presence of C8 in the environment in and around the Facilities. Therefore, the Agencies require the following:

A. Establishment of Groundwater Investigation Steering Team. Ohio EPA EPA Region V

1. A "Groundwater Investigation Steering Team" (GIST) shall be established with members of the team consisting of WVDEP, WVDHHR-BPH, EPA Region III, and DuPont. The WVDEP representative will be the team leader. The objectives and specific tasks of the team are set forth in full in Attachment A of this Consent Order. However, the primary purpose of the GIST will be to oversee an expeditious, phased approach to fulfilling the majority of the requirements set forth in Sections A through C. The work performed with oversight from the GIST shall be funded by DuPont in accordance with Section VIII of this Consent Order.

2. Upon conclusion of key milestones in the tasks set forth in Attachment A, the GIST shall issue interim or final reports setting forth findings of fact and conclusions regarding background data, groundwater monitoring, and plume identification as described in Attachment A. Any groundwater monitoring plan developed pursuant to Attachment A shall survive the termination of this Consent Order and shall be incorporated as a minor permit modification for the Facilities. DuPont reserves the right to request modification of the plans upon renewal of the Facilities' permits.

B. National Pollutant Discharge Elimination System Requirements.

1. Except as occasioned by no-flow conditions, DuPont shall perform monthly sampling for C8 at the Local Landfill at certain outfalls identified in West Virginia/National Pollutant Discharge Elimination System ("WV NPDES") Permit No. 0076538 as Outfalls 101, 004 and 005.

2. Except as occasioned by no-flow conditions, DuPont shall perform monthly sampling for C8 at the Washington Works facility at certain outfalls identified in WV NPDES Permit No. WV0001279 as Outfalls 001, 002, 003, 005, 007, and 105.

3. Except as occasioned by no-flow conditions, DuPont shall perform monthly sampling for C8 at Dry Run Landfill at all outfalls identified in its WV NPDES Permit No. WV0076244.

4. Except as occasioned by no-flow conditions, DuPont shall perform monthly sampling for C8 at Letart Landfill at all outfalls identified in its WV NPDES Permit No. WV0076066.

5. With respect to the requirements of paragraphs VII.B.1 through VII.B.4, all sampling shall be performed pursuant to established EPA guidelines, where applicable, and results shall be delivered to the WVDEP within thirty days of receiving such results. DuPont shall record and report all attempts to sample under no-flow conditions.

6. Within 90 days of the Effective Date of this Consent Order, DuPont agrees to obtain a sample from each surface or alluvial water intake for public water supplies along the Ohio River in the area extending ten river miles downstream of the Washington Works facility and one river mile upstream of the Washington Works facility. If concentrations of C8 above the Detection Limit are found in any sampled public water supply within the upstream or downstream segments initially sampled, the segments within which intakes are to be sampled shall be extended to twenty river miles downstream or two river miles upstream, as appropriate. If concentrations above the Detection Limit are found in any segment so extended, additional sampling will be performed on water intakes within thirty river miles downstream or three river miles upstream, as appropriate.

7. The additional monitoring requirements contained in this subsection shall be incorporated into the Facilities' West Virginia/National Pollutant Discharge Elimination System permits by minor modification. DuPont reserves the right to request a modification of these requirements upon renewal of the permits.

C. Toxicological and Human Health Assessment.

1. DuPont agrees to fund the various tasks set forth below as a part of this Consent Order by establishing an escrow account at a bank agreed to by the Parties, or by some other

means agreed to by the Parties. Disbursements from said escrow shall be authorized by the C8 Toxicity Team Leader and DuPont representative jointly as described below.

2. A C8 Assessment of Toxicity Team ("CAT Team") shall be established with members of the team consisting of representatives of:

WVDEP
WVDHHR-BPH
EPA Region III
NICS
ATSDR
DuPont

3. The WVDEP representative shall be the Team Leader.

4. The individual team members, the tasks of the team, and the team objectives are set forth in full in Attachment C of this Consent Order.

5. Upon conclusion of all the tasks set forth in Attachment C, the CAT Team shall issue a final report setting forth findings of fact and conclusions as to what extent there may be health risks associated with C8 at the Facilities.

D. Emission Modeling Assessment.

1. The following information shall be submitted to the Division of Air Quality ("DAQ") within 30 days of the Effective Date except where a different deadline is provided in this subsection:

a. A complete and accurate list of building dimension parameters for all structures located within the Washington Works facility that have a significant impact on the dispersion of C8 emissions. Significant impact for each structure on the site shall be determined based on the "area of building wake effects" as defined in the EPA User's Guide to the Building Profile Input Program (EPA-454/R-93-038 Revised Feb. 8, 1995).

b. A complete and accurate list of DuPont's current permitted allowable emission rates and confirmed actual C8 emission rates in pounds per year for the year 2000 for all sources located within the Washington Works facility. Each emission point shall be listed according to its stack I.D. and corresponding permit number. For each stack identified above as emitting C8 DuPont shall list all relevant stack parameters to be used in air dispersion modeling.

c. For each emission point (stack) emitting C8, the following information shall be supplied:

i. Phase of C8 (solid, vapor or aqueous solution) at stack conditions.

ii. The particle characterization to be used for modeling including the particle size distribution (microns), the mass fraction of C8 in each particle size category, and the particle density (g/cm^3).

iii. For particulate emissions, scavenging coefficients (hr/s-mm) for both liquid and frozen precipitation to be used for wet deposition modeling based upon the particle size distribution and the EPA's Industrial Source Complex, Version 3 Model Guidance (EPA-454/B-95-003b Sept. 1995) ("ISC Guidance"). DuPont may submit, within 30 days of the Effective Date, information to support the use of the normalized scavenging coefficient in the ISC Guidance (Figure 11 of ISC Guidance) for C8's scavenging coefficients. DAQ shall approve or disapprove with justification in writing, DuPont's submission. Should DAQ disapprove, DuPont shall have the right, within seven days, to request a meeting with DAQ and USEPA to address the deficiencies set forth in DAQ's letter and to request reconsideration of DAQ's decision. Following a meeting of the parties, DAQ shall issue a decision letter regarding C8's scavenging coefficients within seven days of the meeting. DAQ reserves the right to require measurement of C8's scavenging coefficients in its decision and DuPont reserves the right to assert a claim of confidentiality in the event such a measurement is made.

iv. For gaseous emissions, scavenging coefficients (hr/s-mm) for both liquid and frozen precipitation to be used for wet deposition modeling will be provided as a function of droplet size using formulae in the open literature based on the physical properties of C8 and consistent with Section 1.4 of the ISC Guidance. DuPont may submit, within 30 days of the Effective Date, information to support the proposed scavenging coefficient for gaseous emissions including information on the percentage of C8 emissions that would be in gaseous form. DAQ shall approve or disapprove with justification in writing, DuPont's submission. Should DAQ disapprove, DuPont shall have the right, within seven days, to request a meeting with DAQ and USEPA to address the deficiencies set forth in DAQ's letter and to request reconsideration of DAQ's decision. Following a meeting of the parties, DAQ shall issue a decision letter regarding C8's scavenging coefficients within seven days of the meeting. DAQ reserves the right to require measurement of C8's scavenging coefficients in its decision and DuPont reserves the right to assert a claim of confidentiality in the event such a measurement is made.

d. To the extent that the phases exist, a solid, liquid and vapor phase (T-P) diagram for C8 with respect to pressure and temperature. The temperature and pressure ranges shall be representative of exhaust gas conditions before and after control equipment. Estimates of C8's critical properties shall be provided along with measured ranges of phase transition temperatures.

e. In lieu of a binary phase (T-x-y) diagram representing the vapor-liquid equilibrium between water and C8, the solubility and Krafft Point of C8 in aqueous solutions, measured pK value for C8 dissociation in aqueous solutions, and measurements of C8 concentrations or related acids observed when tested in a head space GC at various concentrations, temperatures, and pHs representative of the ranges observed during actual operating conditions. Furthermore a discussion regarding the volatility of C8 in aqueous solutions as a function of pH will be provided. The information in this paragraph shall be submitted to the DAQ within 60 days of the Effective Date.

f. Henry's law coefficient for C8 and a discussion of its dependence on pH. The coefficient shall be defined at various temperatures covering the range observed during actual operations.

g. Any carbon adsorption data in the form of isotherms for C8 adsorption.

DAQ will provide DuPont an opportunity to comment on modeling methodology and assumptions prior to finalizing the modeling results.

2. Any expenses incurred as a result of accurately supplying the information requested above shall be covered by DuPont.

3. Upon submission of the information required by this Subsection VII.D, DAQ reserves the right to disapprove any data if the analytical methodology or quality control procedures are deemed inappropriate.

VIII. REIMBURSEMENT OF COSTS.

1. DuPont agrees to establish an escrow account to fund Reimbursable Costs under this Consent Order. Expenditures from this account shall be made upon joint approval by a duly designated representative of the WVDEP and of DuPont ("designated representatives"). Written notice of such designation shall be sent to the persons identified pursuant to Section XVI of this Consent Order. Prior to the execution of this Consent Order, WVDEP has provided DuPont with an estimate of Reimbursable Costs that WVDEP expects to incur under this Consent Order.

2. Within 10 business days of the Effective Date, DuPont shall deposit in the escrow account funds in the amount of fifty thousand dollars ($50,000). Each expenditure from the escrow account must be supported by an itemized accounting, including invoices and receipts. Said escrow account shall be replenished with additional funds whenever the balance is less than ten thousand dollars ($10,000), or as agreed to by the designated representatives. Any unexpended amount remaining in the escrow account at the conclusion of the work to be performed under this Consent Order shall be returned to DuPont.

3. DuPont's obligation to pay Reimbursable Costs under this Consent Order shall

not exceed two hundred and fifty thousand dollars ($250,000). Except as to Reimbursable Costs which are addressed separately in this section, all other costs incurred by DuPont in carrying out its obligations under Consent Order shall be the sole responsibility and obligation of DuPont.

IX. QUALITY ASSURANCE/QUALITY CONTROL.

All sampling and analyses performed pursuant to this Consent Order shall conform to EPA guidance regarding quality assurance/quality control, data validation, and chain of custody procedures. The laboratory performing the analyses shall be approved by the Parties prior to sampling.

X. C8 REDUCTION PROGRAM.

1. Notwithstanding current permitted emission levels, DuPont agrees to limit overall C8 emissions to the air to no more than actual calendar year 2000 levels on a calendar year basis and shall further provide to the WVDEP monthly emissions reports regarding C8. The reporting requirement contained herein shall be modified to quarterly reports upon the issuance of a Screening Level derived following the procedures set out in Attachment C.

2. DuPont agrees to reduce emissions to the air and discharges to the water of C8 collectively by 50% from actual 1999 levels by December 31, 2003.

3. DuPont shall operate and maintain the filter and carbon bed treatment system at its Washington Works facility with the goal of achieving 90-95% C8 removal efficiency in its major C8-containing wastewater stream.

4. DuPont shall conduct the following construction projects and abide by the specified dates:

a. DuPont shall install an improved scrubber filter to replace recovery device T6IZC on permit R13-815D. Construction shall begin no later than February 28, 2002. Initial operation shall begin no later than the date of start up after the April shutdown, or June 28, 2002, whichever is earlier.

b. DuPont shall modify the stack for emission point T6IZCE so that the emission point elevation is 170 feet above grade. The stack diameter, velocity, and flow rate shall be sized to provide effective dispersion of particulate emissions according to 45 Code of State Rules, Series 20 (Good Engineering Practice as Applicable to Stack Heights). Construction shall begin no later than February 28, 2002. Initial operation shall begin no later than the date of start up after the April shutdown, or June 28, 2002, whichever is earlier. At times when device T6IZC is not operating, permitted emissions from scrubber T6IFC shall be emitted to emission point

T6IZCE.

5. DuPont shall conduct a scrubber optimization and recovery improvement program that shall consist of a study of scrubber operation for device C2DWC2 on permit R13-614A. The study shall be complete by the end of March 2002. Provided the results are encouraging, the company shall implement identified improvements for this device and similar improvements for units C2DTC2 on permit R13-614A, C2EHC2 on permit R13-1953, and C1FSC2 on proposed permit for R13-2365A. Implementation of the improvements for the latter devices will be complete no later than the end of November 2002.

XI. COMPLIANCE WITH SCREENING LEVELS.

1. The following requirements shall apply only if the procedures set out in Attachment C have been followed:

a. No later than 60 days after receipt of notification from the Agencies that data or information developed pursuant to this Consent Order or other information that is recent and valid demonstrates that DuPont's operations have resulted in C8 exposures above the Screening Levels derived following the procedures set out in Attachment C, DuPont shall submit a plan for review and approval by the Agencies that is designed to reduce such exposures to levels below the Screening Levels within a reasonable time (the "Remedial Plan" or "the Plan").

b. Within 30 days of receipt of the Remedial Plan submitted by DuPont, the WVDEP shall, upon consultation with the WVDHHR-BPH and based upon accuracy, quality, and completeness, either approve or disapprove the Plan. If the WVDEP disapproves the Remedial Plan, the WVDEP shall notify DuPont in writing that the Remedial Plan has been disapproved and shall specify the reasons for such disapproval. DuPont shall resubmit the Remedial Plan as revised to address the deficiencies identified in the notice. DuPont's failure to submit an approvable Remedial Plan shall be deemed a violation of this Consent Order.

2. In the event EPA or the WVDEP develops and finalizes a reference dose/screening level for C8 in accordance with applicable statutory and regulatory requirements ("the Regulatory EPA Standard") that would be applicable to Dupont's activities or the Facilities independent of this Consent Order, DuPont's obligations under this Section shall be determined with reference to the Regulatory EPA Standard. DuPont reserves all rights it may have to comment upon, object to, or appeal the Regulatory EPA Standard in proceedings separate and apart from this Consent Order.

XII. COMPLETION OF CONSENT ORDER.

1. Except as to DuPont's obligations under Section XI, this Consent Order and DuPont's obligations hereunder shall terminate upon issuance of a completion letter(s) from the Secretary of the WVDEP or his designee and from the Commissioner of the WVDHHR-BPH to

DuPont. In a timely manner following receipt of a written request from DuPont the respective Agencies shall issue the completion letter(s) to DuPont or shall issue a letter to DuPont detailing the obligations and work that have not been completed in accordance with this Consent Order. The Parties agree that the Agencies' obligation to issue this letter shall be deemed a non-discretionary duty.

2. DuPont's obligation to achieve and maintain compliance with the Screening Levels as provided in Section XI of this Consent Order shall survive the termination of this Consent Order. Such obligation shall terminate only as provided in Section XI or upon agreement of the Parties.

XIII. ADDITIONAL ACTIONS.

The Agencies, individually or collectively, pursuant to their statutory duty and authority, may determine that additional action, beyond the tasks set forth in this Consent Order, is necessary to protect human health and/or the environment. Nothing in this Consent Order shall be construed as restraining or preventing the Agencies from taking such actions. Nothing in this Consent Order constitutes a satisfaction of or release from any claim or cause of action against DuPont for any liability it may have pursuant to the federal Clean Water Act, the federal Clean Air Act, the federal Safe Drinking Water Act, the West Virginia Groundwater Protection Act, the West Virginia Air Pollution Control Act, other statutes applicable to this matter, or West Virginia common law. Nothing in this Consent Order in any way constitutes a modification or waiver of statutory requirements of DuPont and nothing in this Consent Order shall obligate DuPont to undertake any actions not specified herein.

XIV. ENFORCEMENT.

Enforcement of this Consent Order may be had by the filing of a civil action by any of the Agencies in the Circuit Court of Wood County, West Virginia. Violation of the terms and conditions of this Consent Order by DuPont is a violation of the West Virginia Code and may result in enforcement action being taken, including a request for civil penalties as set forth by law. DuPont shall not be liable for violations of this Consent Order due to any "Force Majeure" condition.

XV. CONTENTS OF CONSENT ORDER/MODIFICATION.

The entirety of this Consent Order consists of the terms and conditions set forth herein and in any attachments or exhibits referenced herein. Modification of the terms and conditions of this Consent Order including any modification of timeframes or deadlines established in this Consent Order shall be made only by agreement of the Parties in writing, except that modifications to any

requirement set out in the attachments to this Consent Order may be made upon consensus of the members of the GIST or the CAT Team, as appropriate.

XVI. ADDRESSES FOR ALL CORRESPONDENCE

All documents, including reports, approvals, notifications, disapprovals, and other correspondence, to be submitted under this Consent Order shall be sent by certified mail, return receipt requested, hand delivery, overnight mail or by courier service to the following addresses or to such addresses DuPont or WVDEP may designate in writing.

Documents to be submitted to WVDEP should be sent to:

WV Department of Environmental Protection
1356 Hansford Street
Charleston, West Virginia 25301

Attention: Armando Benincasa, Esq.
Attention: Dee Ann Staats, Ph.D.
Phone No.: (304) 558-2508

Documents to be submitted to WVDHHR-BPH should be sent to:

WV Department of Health and Human Resources
Bureau for Public Health
815 Quarrier Street, Suite 418
Charleston, West Virginia 25301

Attention: William Toomey, Manager of Source Water Assessment Program
Phone No.: (304) 558-2981

Documents to be submitted to DuPont should be sent to:

E. I. du Pont de Nemours and Company
Washington Works
P.O. Box 1217
Parkersburg, West Virginia 26102

Attention: Paul Bossert
Phone No.: (304) 863-4305

and

E. I. du Pont de Nemours and Company
Legal Department, Suite D-71
1007 Market Street
Wilmington, Delaware 19898

Attention: Bernard J. Reilly, Esq.
Phone No.: (302) 774-5445

XVII. AUTHORIZED SIGNATORIES/NON-ADMISSION.

The undersigned representatives state that they have had full and fair opportunity to review this Consent Order and have had opportunity to allow for their counsel to do the same, and therefore enter this Consent Order freely and with full knowledge of its terms and conditions.

The undersigned do hereby confirm that they have the authority to enter into this Consent Order and have the authority to bind their respective party.

Neither the terms of this Consent Order, nor execution thereof shall constitute an admission by DuPont of any fact or of any legal liability. DuPont expressly reserves all rights and defenses that may be available in any proceeding involving third parties or involving WVDEP and WVDHHR-BPH in any other matter.

This Consent Order may be signed in counterparts and shall be effective upon signature of all the Parties below ("Effective Date").

Entered this 14th day of NOVEMBER 2001, by:

WEST VIRGINIA DEPARTMENT OF ENVIRONMENTAL PROTECTION

BY:

William E. Adams

WILLIAM E. ADAMS, DEPUTY SECRETARY
West Virginia Department of Environmental Protection
1356 Hansford Street
Charleston, West Virginia 25301

Entered this 15th day of November, 2001, by:

WEST VIRGINIA DIVISION OF HEALTH AND HUMAN RESOURCES – BUREAU FOR PUBLIC HEALTH

BY:

DR. HENRY TAYLOR, COMMISSIONER
Bureau for Public Health
West Virginia Department of Health and Human Resources
Diamond Building, Room 702
350 Capitol Street
Charleston, West Virginia 25301

Entered this 15th day of Nov, 2001, by:

E. I. DU PONT DE NEMOURS AND COMPANY

BY:

PAUL BOSSERT, PLANT MANAGER

Attachment A

C8 GROUNDWATER INVESTIGATION STEERING TEAM

A team of scientists shall be assembled to assess the presence and extent of C8 in drinking water, groundwater and surface water at and around the DuPont Washington Works facility, and the Local, Letart, and Dry Run Landfills. The Groundwater Investigation Steering Team (GIST) shall include scientists from WVDEP, WVDHHR-BPH, EPA Region III, and DuPont. DuPont shall fund the GIST via an escrow account as provided in Section VIII of the attached Consent Order ("the Consent Order"). Disbursements from this account shall be authorized jointly by the WVDEP GIST leader, and the DuPont representative, Andrew S. Hartten.

A schedule summarizing key GIST tasks, submittals, start and end dates is provided at the end of this document.

GIST Member Organizations/Representatives/General Functions

WVDEP

David Watkins –Groundwater Protection- GIST team leader; escrow funds disbursement oversight; project management and coordination
George Dasher-advisor and technical review
Dee Ann Staats, Ph.D.-advisor

EPA Region III

Garth Connor-science advisor
Jack C. Hwang – Hydrogeologist
Roger Rheinhart-Environmental Engineer

DuPont

Andrew Hartten-Principal Project Leader/Hydrogeologist-technical review, project management and coordination of field investigation activities; escrow funds disbursement oversight.

WVDHHR-BPH

William Toomey-Manager, Source Water Assessment Program- Bureau for Public Health advisor

EPA 01244

GIST Team Objectives and Efforts

The primary objective of the GIST is to efficiently review and direct groundwater and surface water monitoring and investigation activities as prescribed in the Consent Order and in this Attachment. The GIST will utilize a phased approach and employ rapid team decision making toward meeting the requirements in an efficient and timely manner. Unless otherwise directed by the GIST, the tasks outlined below shall be performed by DuPont or its representatives.

The GIST will issue a final report(s) with findings and conclusions regarding groundwater quality in and around the Facilities, and the extent of groundwater contamination in and around the Facilities. The GIST final report shall further make recommendations regarding the need for any further work or actions that need to be taken to assure protection of groundwater quality and human health into the future.

The tasks set forth below and in the Consent Order are the minimum tasks to be performed by DuPont and the GIST pursuant to the Consent Order. Additional tasks may be necessary to assure the goals [full groundwater assessment and C8 impact, plume identification, and receptor identification] of the GIST and the Consent Order are met. Those tasks shall be agreed upon by the GIST.

Key Tasks of GIST

Task A: Groundwater Use and Well Survey/Groundwater Monitoring

- Objectives: Conduct a distance-phased groundwater well and water use survey within a 1-mile (and possibly 2 and 3-mile) radial distance or directionally focused distance of the Washington Works and Local, Letart, and Dry Run Landfills.[1]
- Summary: The phased approach to the water and groundwater well use survey will allow the GIST to focus efforts along established C8 impact transport pathways and cease activities in directions where impacts are not present or where there are minimal concentrations. Data results tables will be generated in a timely manner to allow the GIST to meet, evaluate the data, and determine the next course of action. The GIST will determine when the final groundwater well use survey shall be released.

  DuPont agrees to perform, under the supervision of the GIST and through an agreed-to third party, a groundwater use and well survey identifying and sampling all groundwater wells within a 1-mile radius of the three landfills set forth above and the Washington Works facility. The phased approach may be amended by the GIST should field conditions require, e.g., lack of sampling wells in the 1-mile radius, lack of quality sampling points within the 1-mile radius.

  Sampling shall be performed with the specific purpose of finding and measuring the C8 concentration in water. Should concentrations of C8 found in groundwater wells exceed 1 µg/l within the 1-mile radius, the GIST will determine

1 The water use survey should be in substantially the same format as Attachment B.

whether to expand the well survey to a 2-mile radius, a 3-mile radius, or in a specific direction only. Drinking water wells that measure above 1 µg/l shall be re-sampled at a frequency to be determined by the GIST.

Note: The level of 1 ug/l is utilized in this Consent Order for monitoring purposes only and not as a benchmark for determining risk and this level may be adjusted as determined the GIST in furtherance of the tasks and objectives set forth in this Attachment.

- Timing: The initial well survey within a 1-mile radius of the Facilities will be conducted within 60 days of the Consent Order's Effective Date. Additional well survey activities will be conducted on a schedule to be determined by the GIST.

Task B: Assessment of Existing Groundwater and Surface Water Monitoring Data

- Objectives: Develop and implement a monitoring plan that determines the presence and extent of C8 in drinking water, groundwater, and surface water in and around the Washington Works facility and Local, Letart, and Dry Run Landfills and provide a compilation of all available groundwater/surface water monitoring and hydrogeologic characterization data for each facility, as reflected in Table A-1.
- Summary: The GIST will be tasked with an expedited evaluation of existing historical data and hydrogeologic information in order to prioritize the initial scope of work for continuing groundwater monitoring and any additional investigation activities (e.g., monitoring well installations) required under plume identification. DuPont shall provide all historical data and hydrogeologic information it may have related to the Facilities.
- Timing: Within 30 days of the completion of Task A, the GIST will review all the C8 analytical and facility hydrogeologic information to determine the scope of work for groundwater monitoring and additional investigation. The GIST will then establish a schedule for those activities. It is anticipated that a summary of all historical information for each facility will be submitted to GIST within 60 days of the Consent Order's effective date.

Task C: Plume Identification/Groundwater Assessment

- Objective: Determine the vertical and horizontal extent of any and all C8 impacted groundwater exceeding 1 ug/l or as directed by the GIST, which may determine a lower threshold than 1 ug/l. This task shall also include an assessment of C8 impacted groundwater at Letart Landfill and its impact on the Ohio River and public water supplies along the river.
- Summary: The GIST shall first review historical data and results of Task A to determine an appropriate scope of work. Activities should be prioritized to address groundwater plumes contributing to or with the potential to flow toward off-site receptors, with emphasis on those areas where groundwater is used as a drinking water source.

Upon completion of investigation activities, DuPont shall provide the GIST with predicted groundwater flow and contaminant transport models to assess future plume migration.

- Timing: Upon review of all available information and on a schedule to be determined by the GIST, the GIST will complete an initial evaluation of data to determine and prioritize plume identification.

The timing of the initial phase of plume identification/investigation activities and other activities will be on a schedule established by the GIST. Further investigatory activities needed and agreed to by the GIST to carry out the goals of the GIST shall be performed by DuPont on a schedule established by the GIST.

Modeling

Any and all modeling performed pursuant to this attachment and the Consent Order shall use Groundwater Modeling System, or some other model as approved by the GIST.

TABLE A-1

COMPILATION OF HISTORICAL DATA AND MONITORING PLAN	
a. Dependent upon the availability of certain information, an historical data summary documented in a report that includes:	• A location map. • A site map showing the location of all known groundwater monitoring wells, residential groundwater wells and public water supply within a 1-mile radius the Facilities. • Top-of-groundwater maps. These should span the entire sampling life of the site and should be no less than yearly. If DuPont has only one year's worth of data for a given site, then these maps should be for each quarter; if DuPont has several years worth of data for each site, then these maps can be annual. • C8 concentration contour maps. These should span the entire sampling life of the site and should be no less than yearly. If DuPont has only one year's worth of data for a given site, then these maps should be for each quarter; if DuPont has several years worth of data for each site, then these maps can be annual. • All the C8 groundwater data that has been collected to date. These data should be submitted in easy-to-read tables. These tables should use the method, "<x", to designate all concentrations below the laboratory's minimum detection limit (not "ND" or some other abbreviation), and they should use "mg/" or "µg/" as the unit designation. • If unable to provide the above data, DuPont shall document the reasons why it is unable to gather and submit the information.
b. A groundwater monitoring plan for the Facilities which should address, at a minimum:	• C8 sampling. The samples should be taken from all the wells at the three landfill sites and from a select number of wells at the Washington Works plant. These select wells are to be chosen by the GIST before the groundwater monitoring program begins based on evaluation of historical data/information. The frequency of sampling shall be monthly for the first four months following the Effective Date and quarterly thereafter. Any new wells required for monitoring or plume identification purposes will be integrated in each site's groundwater monitoring program on a schedule agreed to by the GIST.

- Report of Results. Reporting should be quarterly and to the WVDEP Groundwater Program at the following address.

  WVDEP Division of Water Resources
  Groundwater Program
  1201 Greenbrier Street
  Charleston, West Virginia 25311
  Re: DuPont/C8 monitoring.

- Each report should include the following:

  (a) A site location map.

  (b) A site map showing the groundwater monitoring well locations.

  (c) A top-of-groundwater map.

  (d) A C8 concentration map.

  (e) Groundwater elevation and well screen data.

  (f) A table of all the historical C8 sampling data. Note; where available information allows, abbreviations should not be used to designate No Detect concentrations and the units "ppb" and "ppm" should not be used.

  (g) Laboratory analysis sheets.

  (h) Chain of custody records.

Attachment B

GROUNDWATER WELL USE SURVEY

Name: _____

Address: _____
_____
_____

Phone: _____

Best Time to Contact Owner: _____

1. Do you have one or more water well(s) on this property? (It need not be in use currently.) If no, stop now and return survey. Yes _____ No _____

   County Water Well Permit No. _____

2. Is the well(s) currently (circle one) used unused or filled in?

3. Is the well(s) used for drinking water? Yes _____ No _____

4. Is this well(s) used for other purposes? If yes, please specify uses below:

_____
_____
_____
_____

5. What is the approximate frequency of use? Circle One:

   Daily Weekly Monthly Summer

6. Date last used? _____

7. Is there a pump in the well? Yes _____ No _____

8. Is there a conditioner, softener, chlorinator, filter, or other form of treatment for the system? Yes _____ No _____

If so, what is the form of treatment? _____

9. Is there any faucet where water does not first pass through the treatment system?
Yes _____ No _____

If yes, is it (circle one) inside or outside?

10. What year was the well constructed? _____

11. Please provide the following information regarding the well(s) if known: (circle one)

A. Total Depth (feet below ground surface):

30-60 60-90 90-120 120 or more

B. Casing Type:

PVC steel stone none other _____

C. Well Construction:

dug drilled open or uncased bedrock

D. Screened Interval (length in feet):

0-10 10-20 20-30 30-60 60 or more

E. Well Diameter (inches):

0-6 6-12 12-24 24 or more

Attachment C

C8 ASSESSMENT OF TOXICITY TEAM

A team of scientists shall be assembled to assess the toxicity and risk to human health and the environment associated with exposure to ammonium perfluorooctanoate (C8) releases from DuPont's activities. The C8 Assessment of Toxicity Team (CAT Team) shall include scientists from academia, government, non-profit organizations, and industry. The CAT Team also shall include the WVDEP Environmental Advocate, Pam Nixon, as a representative of West Virginia's citizens.

The WVDEP, utilizing funds from an escrow account funded by DuPont, shall contract with a non-profit organization, the National Institute for Chemical Studies (NICS), for the services described herein. Point of contact for the NICS shall be Jan Taylor, Ph.D. The NICS shall subcontract with Marshall University's Center for Rural and Environmental Health for services in risk communication provided by James Becker, M.D. and his staff. Dr. Becker shall familiarize himself with the toxicity of C8, the work performed by TERA as described herein, and attend public meetings to provide expertise in risk communication. The NICS shall subcontract with the non-profit scientific organization, Toxicology Excellence for Risk Assessment (TERA) whose point of contact is Joan Dollarhide, Ph.D. The TERA shall provide services in toxicology and risk assessment. Work assignments, tasks, and deliverables are described below.

CAT Team Member Organizations/ Representatives[1]/ General Functions

WVDEP

Dee Ann Staats, Ph.D. - Science Advisor - team leader; escrow funds disbursement oversight; project management and coordination; toxicology/risk assessment and communication;

Pam Nixon - Environmental Advocate - advisor;

NICS

Jan Taylor, Ph.D. –contractor administrative oversight;

James Becker, M.D. (Marshall University) - consultant in risk communication;

TERA (point of contact: Joan Dollarhide, Ph.D.)- consultant in toxicology/risk assessment;

[1] The parties may, in their discretion, elect to substitute their representatives with persons of similar qualifications.

DuPont

Gerald Kennedy, Director of Applied Toxicology and Health, Haskell Laboratory - reviewer toxicology; escrow funds disbursement oversight;

John Whysner, M.D. – toxicology/risk assessment and communications;

Paul Bossert – Washington Works Plant Manager – communications;

The following members of the CAT Team shall act as reviewers or advisors.

WV Department of Health and Human Resources – Bureau for Public Health (WVDHHR-BPH)

William Toomey – Manager, Source Water Assessment Program - advisor;
Barbara Taylor – Director, Office of Environmental Health Services - advisor;
Local representative - advisor;

Environmental Protection Agency (EPA)

Headquarters - Jennifer Seed – reviewer and advisor toxicology;
Region III Philadelphia -
Samuel Rotenberg, Ph.D. – reviewer and advisor toxicology/ risk assessment;
Garth Connor – advisor hydrogeology;
Roger Reinhart – reviewer and advisor Safe Drinking Water Act;
Cincinnati - John Cicmanec, DVM – reviewer and advisor toxicology;

Agency for Toxic Substances and Disease Registry (ATSDR)

Atlanta - John Wheeler, Ph.D. - reviewer and advisor in toxicology/ risk assessment;
Philadelphia - Lora Werner - coordinator for ATSDR;

Non-CAT Team Efforts

Other efforts are currently underway which may produce information for the CAT Team to utilize. The CAT Team will coordinate and communicate closely with these other efforts. These include:

1. Dupont's air modeling of C8 emissions from the Washington Works plant;

2. WVDEP's air modeling of C8 emissions from the Washington Works plant;

3. USEPA Draft Hazard Assessment which summarizes the available toxicity information regarding C8, to the extent completed prior to the assessment contemplated herein;

4. ATSDR's Health Consultation that estimates the risk to the community associated with C8 in drinking water from the Lubeck Public Service District, to the extent completed prior to the assessment contemplated herein.

5. Existing C8 concentrations in Lubeck Public Service District data.

6. Groundwater C8 Analysis (see GIST activities described in Attachment A) and Well Use Survey (see example survey in Attachment B) at the residences in the area of the 3 landfills and the Washington Works Plant.

Tasks of CAT Team

The tasks to be performed by the CAT Team are described briefly in Table 1, and in more detail below. These tasks are discussed below within the context of a Scope of Work for both Dr. Becker and for TERA as well.

Tasks of the CAT Team shall be organized into three phases. Phase I includes those tasks necessary to prepare for and hold the first public meeting. In Phase II, TERA shall conduct such scientific tasks as: reviewing available toxicity and epidemiological studies; developing Provisional Reference Doses and Screening Levels for protection of human health; evaluating existing information relative to ecological health; and conducting one general risk assessment involving comparisons of exposure concentrations to Screening Levels, for the three landfills and the Washington Works Plant, and the Lubeck Public Service District. TERA shall prepare a report on their findings. Phase III includes those tasks necessary to prepare for and hold the second public meeting. The results of the C8 groundwater analysis and risk assessment shall be presented in the second public meeting.

No communication between Dupont representatives and NICS, Dr. Becker, or TERA shall be permitted without the participation of Dr. Staats. All information will be provided to Dr. Becker and TERA by WVDEP; thus, all information contributed to the effort by Dupont shall be sent in triplicate to Dr. Staats for forwarding to Dr. Becker and TERA.

Phase I TASK A-1: First Public Meeting

Two public meetings are anticipated for this project. The First Public Meeting shall occur in Phase I for the purposes of introducing the CAT Team and other involved parties to the public; relating historical information on previous concentrations of C8 in Lubeck Public Service District water supply; informing the citizens of the ensuing activities; and inviting the public to participate by cooperating with sampling and survey efforts in the Groundwater C8 Analysis and Well Use Survey. In order to prepare for the

First Public Meeting, CAT Team members shall familiarize themselves with the available toxicological information concerning C8.

A CAT Team meeting shall be held immediately prior to the first public meeting to: (1) conduct a site visit to the three landfills and the Washington Works Plant, and surrounding residential areas; (2) discuss the toxicity of C8 and other pertinent data; (3) prepare an agenda for the public meeting; (4) coordinate and prepare for the public meeting. Finally, the First Public Meeting will be held and public questions and comments will be recorded by WVDEP.

TABLE 1. TASKS OF CAT TEAM
Task A: Public Meetings (two meetings are anticipated) **Objective:** to inform the local citizens of the following: (in Meeting #1) intent to perform a groundwater well use survey and analysis for C8; intent to develop Screening Levels; and to ask for their cooperation in conducting the water use survey; and (in Meeting #2) results of survey, chemical analysis, and risk assessment. Note that an interim public meeting may be required should six months pass from the first public meeting and the CAT Team Final Report has not been issued. **Primary Responsibility:** Staats
Task B: Development of Provisional Reference Doses **Objective:** to develop Provisional References Doses for C8 for the inhalation and ingestion (and dermal, if possible) routes of exposure. **Primary Responsibility:** TERA
Task C: Development of Screening Levels Based on Protection of Human Health **Objective:** to utilize the Provisional Reference Doses to develop human health risk-based Screening Levels for C8 in air, water, and soil. Note a determination of the potential carcinogenicity of C8 will be conducted as well. **Primary Responsibility:** TERA
Task D: Ecological Data Review **Objective:** to review available information to determine whether sufficient studies have been performed and data have been collected to develop screening criteria for ecological receptors. **Primary Responsibility:** TERA
Task E: Draft Report and Final Report **Objective:** to present and discuss the results of the above tasks. **Primary Responsibility:** TERA

Phase II Tasks B, C, D, and E Development of Provisional Reference Doses and Screening Levels, and Risk Assessment

In Phase II, TERA shall conduct the toxicological and risk assessment activities. After having reviewed the toxicological information regarding C8 provided by WVDEP, TERA shall consult with toxicologists on the CAT Team, as coordinated by Dr. Staats, regarding its proposed approach for this project. Following such consultation, TERA

shall develop Provisional Reference Doses for C8 for the oral, inhalation, and dermal (if possible) routes of exposure. Then TERA shall calculate Screening Levels for water, soil and air based on the risk factors they have estimated. TERA shall perform one general risk assessment involving comparison of exposure concentrations to Screening Levels for the three landfills and the Washington Works Plant, and the Lubeck Public Service District water supply, that focuses on current risk to human health, including workers and residents. This risk assessment shall include: (1) identification of reasonably anticipated land use, surface water and groundwater use; (2) identification of receptors; (3) identification of exposure pathways; (4) identification of exposure concentrations; and (5) comparison of exposure concentrations to appropriate Screening Levels. TERA shall utilize data obtained from the other efforts discussed above such as air modeling; groundwater C8 concentrations in residential and public wells; residential groundwater well use survey; the USEPA's Draft Hazard Assessment; and ATSDR's Health Consultation (if available). TERA also shall review available information to determine whether sufficient studies have been performed and data have been collected to develop screening criteria for protection of ecological health, particularly aquatic life. TERA shall prepare a draft and a final document that discusses the results of their efforts and summarizes the data utilized from other efforts. As the tasks of the CAT Team and other involved parties' progress, data gaps and research recommendations may become evident. These shall be included in TERA's report as suggestions for further research to elucidate the toxicity of C8.

Phase III Second Public Meeting

The purpose of the Second Public Meeting is to present to the citizenry the results of the efforts of the GIST and CAT Teams including C8 concentrations in groundwater from residential wells and public wells the screening levels and the general risk assessment. Air modeling results of the efforts of WVDEP and Dupont will be discussed also. The WVDEP will address any further actions that may be necessary.

SCOPE OF WORK FOR
JAMES BECKER, M.D.

Dr. Becker is a medical doctor specializing in environmental health at the Marshall University School of Medicine Center for Rural and Environmental Health. He will be assisting the WVDEP in his specialty area of risk communication at the two anticipated public meetings. The specific tasks assigned to Dr. Becker are described below.

Phase I Task A-1: First Public Meeting

Dr Becker will assist in preparation for the first public meeting, and attend the meeting providing expertise in risk communication . He will familiarize himself with the available toxicological data, which will be provided to him by WVDEP, with particular emphasis on the epidemiological studies. Note that the toxicological data already has been summarized in the Draft Hazard Assessment prepared by USEPA. No literature search or document retrieval will be required. Specific subtasks required in Phase I to prepare for the first public meeting are described below:

Subtask 1 – Familiarization with toxicological data provided by WVDEP including but not limited to:

a. 8 compact discs of information provided to USEPA under TSCA by 3M Corp (note only a small portion of this information concerns C8);
b. Draft Hazard Assessment document from USEPA;
c. ACGIH Threshold Limit Value (TLV).
d. Journal articles and other information provided by WVDEP.

Subtask 2 – Attend a meeting prior to the first public meeting to:

a. conduct a site visit of the 3 landfills and the Washington Works Plant, and local residential areas;
b. discuss and prepare an agenda;
c. discuss the toxicology and risks associated with C8 with the other CAT Team members.

Subtask 3 – Attend First Public Meeting

Phase III Task A-2 Second Public Meeting

Dr Becker will assist in preparation for the second public meeting, and attend the meeting providing expertise in risk communication. The following subtasks will be required:

Subtask 1 – Familiarization with the toxicological and risk assessment report prepared by TERA;

Subtask 2 – Attend a meeting prior to the second public meeting to:

a. discuss the toxicology and risks associated with C8 with the other CAT Team members;
b. discuss and prepare an agenda.

Subtask 3 – Attend Second Public Meeting

Note that the second public meeting is assumed to be the final public meeting; however, results of data collection may warrant additional public meetings and an expansion of the Scope of Work.

SCOPE OF WORK FOR TERA

TERA (Toxicology Excellence for Risk Assessment) is a non-profit organization that applies sound toxicological data to the risk assessment process to find common ground between environmental, industry, and government groups. TERA will be providing services in toxicology and risk assessment. TERA scientists will be developing risk factors and screening criteria; and conducting one general risk assessment for the 3 landfills, Lubeck Public Service District water supply and the Washington Works Plant. The specific tasks assigned to TERA are described below.

Phase II Tasks B, C, D, and E: Development of Provisional Reference Doses and Screening Levels, and General Assessment of Risk

Subtask 1 – TERA staff will familiarize themselves with the toxicological data provided to by WVDEP. No literature search or document retrieval will be required. Toxicological data to be provided to TERA shall include but is not limited to the following:

a. 8 compact discs of information provided to USEPA under TSCA by 3M Corp (note only a small portion of this information concerns C8);
b. USEPA Draft Hazard Assessment for C8;
c. Journal articles and other information submitted to WVDEP by DuPont.

Subtask 2 – TERA staff will:

a. identify all possible critical toxicological studies suitable for developing Reference Doses for the oral, inhalation, and dermal (if possible) routes of exposure;
b. outline methodology for developing said Reference Doses and for developing Screening Levels for air, water, and soil based on said Reference Doses corresponding to each critical study identified in subtask 2-a;
c. convene a meeting at the TERA facility in Cincinnati, Ohio, to present their findings in subtask 2-a and 2-b, and consult with CAT Team toxicologists as coordinated by Dr. Staats;
d. finalize Reference Doses and Screening Levels based on recommendations of the CAT Team toxicologists as coordinated by Dr. Staats.

Subtask 3 – TERA shall conduct one general risk assessment for the three landfills and Washington Works Plant, and the Lubeck Public Service District water supply based on current risk to human health. This risk assessment shall include:

a) identification of reasonably anticipated land use, surface water and groundwater uses;

b) identification of receptors;
c) identification of exposure pathways;
d) identification of exposure concentrations;
e) comparison of exposure concentrations to appropriate Screening Levels;

TERA shall utilize the following data in the risk assessment process:

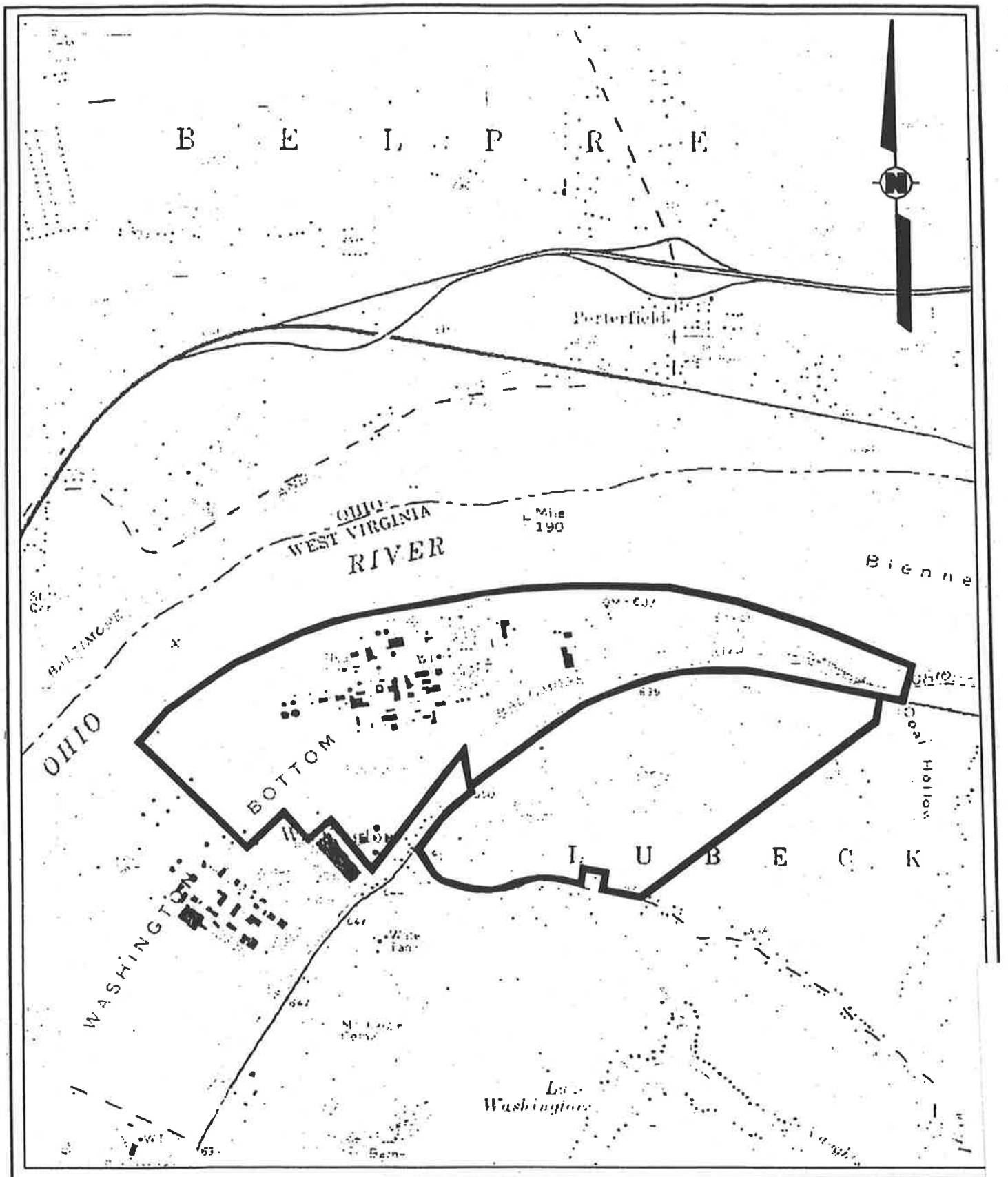
a) air modeling data from DuPont;
b) air modeling data from WVDEP;
c) water use data from the Well Use Survey;
d) groundwater data from the Groundwater Well Analysis of C8 for residential wells;
e) drinking water data from Lubeck Public Service District wells;
f) any available ATSDR Health Consultation that assesses potential health effects from exposure to C8 in public supply drinking water.

Subtask 4 – TERA shall review the ecological data and determine whether there is sufficient information to support the development of a C8 Screening Level for protection of ecological health

Subtask 5 – TERA shall compile and discuss the results of the above tasks into a comprehensive report (draft and final versions), which also refers to and provides a brief summary of the following:

a) USEPA's Draft Hazard Assessment of C8;
b) DuPont's air modeling data;
c) WVDEP's air modeling data;
d) groundwater data from the Groundwater C8 Analysis and Well Use Survey of Local Residents, and Lubeck Public Service District;
e) ATSDR Health Consultation that assesses potential health effects from exposure to C8 in public supply drinking water, if available.

Additionally, TERA shall include in the report any insights or recommendations for future research gleaned during this process that would further elucidate the toxicity of C8. Also, TERA shall provide in the report of a summary discussion of the relevance the carcinogenicity of C8 in rats to humans.



Source: USGS Little Hocking, Ohio – Quadrangle

Corporate Remediation Group
An Alliance between DuPont and URS Diamond

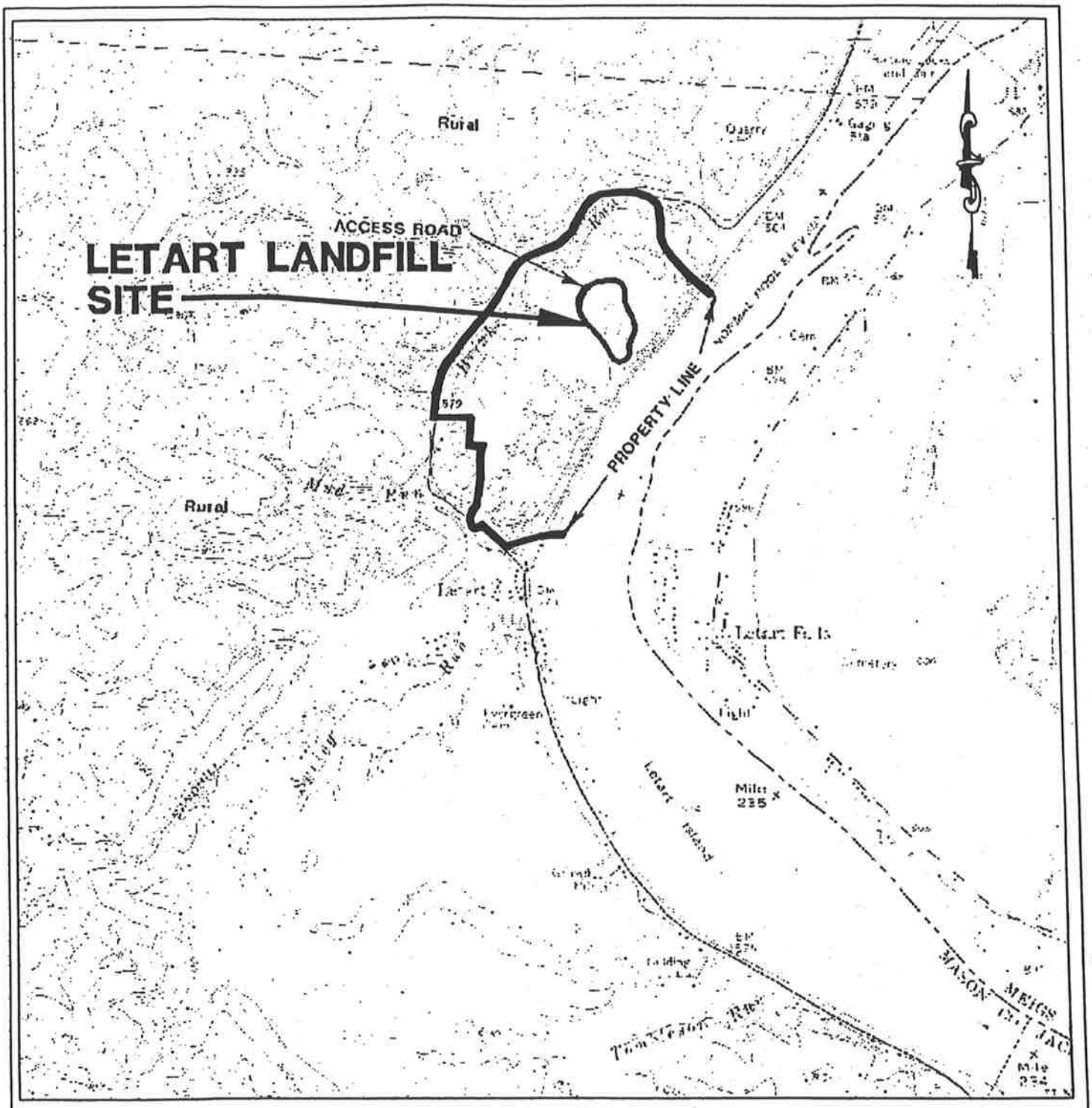
EXHIBIT 1

SITE LOCATION MAP

DuPont Washington Works
Washington, West Virginia

SCALE	DESIGNED	DRAWN	CAD FILE NO.
Not to scale	DEL	DEL	SITE_LOC
DATE	CHECKED	APPROVED	FIGURE
8/27/01	M. HOLLIDAY		1

EPA 01261



SOURCE: NEW HAVEN, WV-OHIO QUADRANG

DUPONT

Corporate Remediation Group

An Alliance between DuPont and The E-C Diamond Group

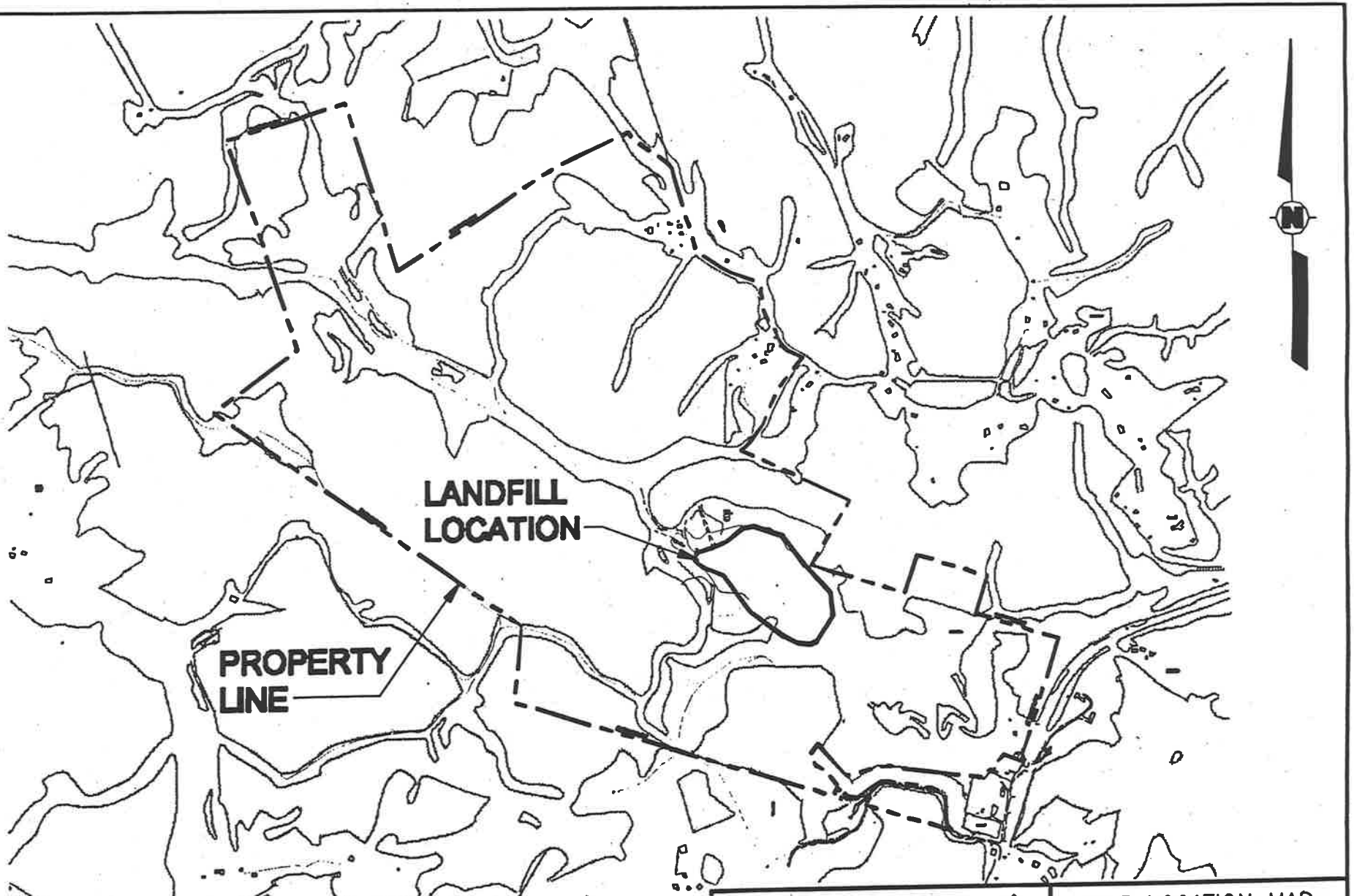
EXHIBIT 2

SITE LOCATION MAP

Letart Landfill Site
Parkerburg, WV

SCALE	DESIGNED	DRAWN	CAD FILE NO.
As shown	TDL	DEL	72684003
DATE	CHECKED	APPROVED	FIGURE
12/21/0			1

EXHIBIT 3



DUPONT

Corporate Remediation Group
An Alliance between DuPont and URS Diamond
Barley Mill Plaza, Building 27
Wilmington, Delaware 19805

SITE LOCATION MAP

Dry Run Landfill
Wood County, West Virginia

SCALE	DESIGNED	DRAWN	CAD FILE NO.
As shown		DEL	Dry_Run_site
DATE	CHECKED	APPROVED	FIGURE
10/1/01			1

EPA 01263

DuPont
Washington Works
P. O. Box 1217
Parkersburg, WV 26102-1217

DUPONT

February 11, 2002

Michael Baker, Chief
Division of Drinking and Ground Waters
Post Office Box 1049
Columbus, OH 43216-1049

Dear Mr. Baker:

On behalf of E. I. du Pont de Nemours and Company ("DuPont") I want to thank you for meeting with us on February 1, 2002, to discuss issues related to the discovery of ammonium perfluorooctanoate (APFO, also known as C8) in the groundwater at the Little Hocking Water Association well field. We found the exchange to be very constructive.

Pursuant to our discussions at that meeting, we have raised with the West Virginia Department of Environmental Protection ("WVDEP") the possibility of representatives of the Ohio Environmental Protection Agency ("Ohio EPA") participating on the Groundwater Investigation Steering Team ("GIST"). As you know, the GIST was formed pursuant to the multi-media consent order ("MMCO") that was issued to DuPont by WVDEP and the West Virginia Department of Health and Human Resources, effective November 15, 2001. The purpose of the GIST is to oversee "an expeditious and phased approach" for the assessment of the presence and extent of C8 contamination in drinking water, groundwater and surface water at and around DuPont's Washington Works and other DuPont facilities in West Virginia. The WVDEP representatives with whom we have spoken have agreed to give consideration to our request, and we are awaiting their reply.

Regardless of the position taken by WVDEP in response to the request for participation by Ohio EPA on the GIST, DuPont is prepared to undertake voluntarily a well survey and sampling of private groundwater wells in the area of the Little Hocking Water Association well field following the protocol that has been establish under the MMCO. This would include a groundwater use and well survey identifying and sampling all groundwater wells within a 1-mile radius of the well field.

We are prepared to initiate this sampling as soon as the logistics can be worked out with all appropriate governmental entities. We look forward to working with you and other representatives of Ohio EPA in this matter.

Very truly yours,

David M. Rurak
Safety Health & Environmental Manager
DuPont Fluoroproducts

EPA 01264

CERTIFICATE OF SERVICE

I certify that on the date noted below, I delivered by hand the original of this Order on Consent to the Regional Hearing Clerk, U.S. EPA Region III, and one copy to the addressees below as indicated:

VIA FACSIMILE

Bernard J. Reilly, Esq.
DuPont Legal, Room D 7082
1007 Market Street
Wilmington, DE 19898

Paul Bossert, Plant Manager
DuPont Washington Works Facility
Route 892
Washington, WV 26181

Dated: 3/14/02

Janet E. Sharke (3RC00)
Senior Asst. Regional Counsel
Office of Regional Counsel
EPA, Region III
1650 Arch Street
Philadelphia, PA 19103-2029
215-814-2689 (phone)
215-814-2601 (fax)

DOCUMENT 51

FINAL

AMMONIUM PERFLUOROOCTANOATE (C8)

ASSESSMENT OF TOXICITY TEAM (CATT) REPORT

August 2002

Department of Environmental Protection - *promoting a healthy environment*

DOCUMENT 51

EPA 01266

EXECUTIVE SUMMARY

Pursuant to a consent order signed November 14, 2001 between the West Virginia Environmental Protection and Health and Human Resources departments, and E. I. Du Pont de Nemours, Inc. (DuPont) the C8 (ammonium perfluorooctanoate) Assessment of Toxicity Team (CATT) was established to:

(1) determine risk-based human health protective screening levels (SLs) for this unregulated chemical in air, water, and soil;

(2) provide health risk information to the public; and

(3) determine an ecological health protective SL for C8 in surface water.

To date, two public meetings have been held in the vicinity of the DuPont Washington Works facility located near Parkersburg, West Virginia. Also, a team of 10 expert toxicologists have met and determined human health provisional risk factors for the oral and inhalation routes of exposure, and calculated health protective SLs based on these risk factors using Region 9 U.S. Environmental Protection Agency standard methodology. The results of the CATT's investigation are presented in summary below. The ecological SL for surface water currently is still in development. An addendum to this report is expected to be released in Fall 2002 presenting the surface water SL findings.

The methodology, overall process, and rationale utilized by the CATT to develop these risk factors and SLs are discussed, the members are listed, and a synopsis of the events leading to the consent order are presented herein. The intent of this report is to document the process and conclusions of the CATT in an effort to provide to the public a record of these activities. It is not intended to be a summary of all the toxicology information available on C8.

The risk factor or Reference Dose (RfD) for the oral route of exposure determined by the CATT for C8 was 0.004 milligrams per kilogram of body weight per day (mg/kg-day). A risk factor for the inhalation route of exposure or the Reference Concentration (RfC) of 1 micrograms per cubic meter of air ($\mu g/m^3$) was determined. The RfD or RfC is defined by EPA as an estimate (with uncertainty spanning perhaps an order of magnitude or greater) of a daily exposure level for the human population, including sensitive subpopulations, that is likely to be without an appreciable risk of deleterious effects during a lifetime. Based on the oral RfD, health protective SLs were calculated for water of 150 parts per billion (ppb), and for soil of 240 parts per million (ppm). Based on the inhalation RfC, a health protective SL of 1 $\mu g/m^3$ was derived for air.

ACKNOWLEDGEMENTS

The West Virginia Department of Environmental Protection wishes to thank the following agencies and organizations that joined us as primary participants in this investigation: West Virginia Department of Health and Human Resources; U.S. Environmental Protection Agency (EPA) Region 3, Office of Research and Development (ORD) and Headquarters; E. I. Du Pont de Nemours, Inc. (as well as their employees, consultants - Potesta & Assoc., Inc., laboratory – Exygen Research, Inc., and attorneys); Marshall University; Toxicology Excellence for Risk Assessment (*TERA*); and Menzie Cura & Assoc., Inc. Specifically, we thank the following EPA personnel for their technical support and camaraderie: Karen Johnson, Janet Sharke, Garth Connor, Roger Reinhart, and Mary Dominiak. We also thank the following organizations for their cooperation: EPA Region 5, Ohio EPA, and the National Institute for Chemical Studies.

We thank all the individual members of the C8 Assessment of Toxicity Team (CATT) for their participation and cooperation. In particular, we thank the following CATT members:

- James Becker, M.D., and Tracy Smith, M.S., of Marshall University for their professionalism, scientific knowledge, and common sense approach to communicating environmental health risks to the public.

- The toxicologists who embarked on an expedition to find the truth, the ambition of all noble scientists:

EPA

John Cicmanec, D.V.M., M.S., USEPA ORD
Samuel Rotenberg, Ph.D., USEPA Region 3
Jennifer Seed, Ph.D., USEPA Headquarters

TERA

Michael Dourson, Ph.D.
Joan Dollarhide, MS, MTSC, JD
Andrew Maier, Ph.D., CIH
Dan Briggs, Ph.D., DABT (note taker)

Agency for Toxic Disease Registry

John Wheeler, Ph.D.

DuPont

Gerald Kennedy
John Whysner, M.D., Ph.D., D.A.B.T. (consultant)

Invited guests:

John Butenhoff, Ph.D., 3M (study scientist)
Jim Sferra, MS, OEPA (observer)

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1.0 INTRODUCTION

The investigation described herein was conducted pursuant to the November 14, 2001 Consent Order Number GWR-2001-019 between the West Virginia Departments of Environmental Protection (DEP) and Health and Human Resources (DHHR), and E. I. Du Pont de Nemours, Inc. (DuPont). A copy of this consent order is included as Attachment I. These actions were instigated by the presence of an unregulated chemical, ammonium perfluorooctanoate commonly called C8, in the Lubeck, W.Va. public water supply which is near the DuPont Washington Works (WW) facility in Washington, W.Va. A site map is included in Attachment IIc.

The consent order established two scientific teams: (1) the C8 Assessment of Toxicity Team (CATT), and (2) the Groundwater Investigation Steering Team (GIST). The CATT was tasked with investigating the toxicity of C8; developing provisional risk factors for the inhalation, dermal, and oral routes of exposure; and establishing human health protective screening levels (SLs) for air, water, and soil; investigating the ecological toxicity of C8 and determining an ecological health protective SL for surface water; and with communicating health risk information to the public. In the consent order DuPont agreed to meet these SLs at their WW facility, once developed, and that these SLs would remain in effect until superseded by U.S. Environmental Protection Agency (EPA) guidance. The CATT's activities and findings regarding the toxicity of C8, development of risk factors and SLs are presented in detail in Section 2 of this report. Slides presented at the two public meetings held thus far are provided in Attachment II. The investigation into the ecological toxicity of C8 and surface water SL development is scheduled for completion in Fall 2002. When finished, the surface water will be presented in an addendum to this report.

The GIST was established by the consent order to determine the extent and concentration of C8 in both groundwater and surface water. The activities of the GIST continue as of the issuance of this CATT report. The GIST will issue a report on the C8 analytical data for groundwater and surface water when that work is finished, scheduled for early 2003. Interim reports are available through the DEP Division of Water Resources (DWR). The groundwater investigation focused not only on the WW plant, but also on areas where C8 had been disposed, including the Local Landfill (on WW property), Dry Run Landfill (near the WW plant), and the Letart Landfill (30 miles south of the WW plant). Maps of the one-mile radius study area around these locations are included in the presentation of interim results at the second public meeting provided in Attachment IIc.

Summarized findings to date by the GIST are compared to the health protective water SL developed by the CATT in Section 3.0. Results of air dispersion modeling efforts thus far conducted by the DEP Division of Air Quality (DAQ) are compared to the air SL in Section 3.0 as well.

Background

The DuPont WW plant is located approximately 10 miles southwest of Parkersburg, W.Va. along state Route 61 in the rural hamlet of Washington, W.Va. This facility was established in the 1940s and currently is one of the largest DuPont enclaves in the world. DuPont has used C8 at this facility for more than 50 years as a surfactant in various manufacturing processes, including the production of Teflon. "C8" is the 3M trade name for its product that contains ammonium perfluorooctanoate (APFO) (CAS # 3825-26-1). In biologic media, APFO quickly dissociates to perfluorooctanoate, which is the anion of perfluorooctanoic acid (PFOA). The PFOA form has been identified as potentially toxic to animals. Throughout this report, C8 is used as terminology to include C8, APFO, or PFOA.

The DEP became aware of and began investigating the presence of C8 in the Lubeck, W.Va. public water supply in November 2000. In Spring 2001, DEP received a letter requesting a formal agency investigation into DuPont's environmental releases of C8 and the presence of C8 in the Lubeck drinking water from attorneys representing a few citizens residing in proximity to the WW plant. The Lubeck public water supply well field lies approximately 3 miles south of the DuPont WW plant. Also around this time, DEP became aware that C8 was chemically similar to perfluorooctane sulfonate (PFOS), another perfluorocarbon manufactured by 3M, and that 3M had recently removed their Scotchguard product from the marketplace because it contained PFOS. From U.S. EPA Region 3 and Headquarters, DEP learned that 3M had undertaken a significant research effort into the toxicity of perfluorocarbons, particularly PFOS and including C8; that perfluorocarbons were potentially more toxic than previously thought; that 3M was submitting the new data to EPA under the Toxic Substances Control Act (TSCA); and that these data were publicly available under Administrative Record 226 (AR226). Additionally, DEP learned that DuPont was submitting toxicity data on C8 to EPA, as well.

DEP gathered data and met with DuPont and met with citizens attorneys in Spring 2001. The DEP, which regulates groundwater in West Virginia, was joined in the investigation by the DHHR, which regulates drinking water. The DHHR requested support from EPA Region 3 to enforce the National Safe Drinking Water Act. At the request of these agencies, DuPont supplied information regarding C8 and its use in manufacturing processes, its toxicity, and emissions. After several months of investigation and discussions, a consent order was signed in November 2001. A copy of the consent order is provided in Attachment I. It describes the tasks and members of the CATT and GIST. The DEP informed the public of the consent order and scheduled a public meeting to discuss the order.

The DEP held it's first public meeting regarding C8 on November 29, 2001 at Blennerhassett Junior High School which is located near the Lubeck and Washington communities. The meeting was spearheaded by the CATT and the GIST. The purpose of the meeting was to inform citizens of: (1) the requirements of the consent order; (2) the members and activities of the GIST; (3) their assistance was required to fill out and return a water use survey if they had groundwater wells, cisterns, or springs (particularly those used for drinking water), and to allow sampling of these water sources; (4) the members and activities of the CATT; (5) the available information regarding the toxicity of C8; and (6) the known current levels of C8 in the Lubeck public water supply, which were below 1 part per billion (ppb). At this meeting, James Becker, M.D. of Marshall University spoke regarding environmental exposures and risks in general, and Dee Ann Staats, Ph.D. (DEP) explained the CATT and GIST activities, the consent order, and known toxicity of C8. The slides from both presentations are provided in Attachment IIa.

By the end of January 2002, contractors were in place to assist the CATT and the GIST in their tasks. The GIST was headed by DEP and had members from DHHR, EPA, and Dupont. The CATT was headed by DEP and had members from DHHR, EPA, DuPont and the Agency for Toxic Substances Disease Registry (ATSDR). The DEP contracted with the National Institute of Chemical Studies (NICS), a nonprofit organization, which subcontracted the human and ecological toxicology work to the Toxicology for Excellence in Risk Assessment (*TERA*) group, also a nonprofit, which subcontracted the ecological toxicology work to Menzie Cura & Assoc., Inc. (MC). Both *TERA* and MC are well respected in the field of toxicology. The NICS subcontracted the risk communications tasks to Marshall University.

In March 2002, EPA Regions 3 and 5 signed a consent order with DuPont requiring the provision of alternative water to any resident in West Virginia or Ohio with C8 in drinking water at levels above 14

ppb. The 14 ppb was an interim value in effect until the water SL was developed by the CATT. This value was taken from the final report by ENVIRON Int. Corp. (a consulting firm hired by DuPont) titled "A Hazard Narrative for Perfluorooctanoate (PFOA)", January 2002. An earlier draft, "A Review of the Toxicology of Perfluorooctanoate (PFOA)", November 2001, had proposed a drinking water value of 210 ppb. However, DEP's toxicologist, Dr. Staats, expressed concern over some of the assumptions made in the calculation of the 210 ppb to DHHR and EPA Region 3. The outcome of these discussions was a decision that a very conservative approach should be taken in the interim until the CATT water SL was developed. Therefore, 14 ppb was accepted as the interim water SL for alternative water provision. Note that this consent order was jointly signed by two regions of EPA because West Virginia is in Region 3 and Ohio is in Region 5. During the investigation, C8 had been found in the Little Hocking, Ohio public water supply. Also, note that DEP and DHHR invited Ohio EPA to join the CATT and GIST as observers, but not as members because this would have required renegotiating the consent order between West Virginia and DuPont.

TERA was assigned by DEP to review and compile the C8 toxicological information provided by DEP and to prepare for and hold a meeting of the CATT toxicologists during which the provisional risk factors and health protective SLs would be derived. The CATT toxicologists panel was comprised of 10 expert scientists with a collective span of experience of over 175 years and many specialties including endocrinology, veterinary medicine, cancer, and risk assessment.

TERA's efforts are described further in Section 2.1. By mid April 2002, *TERA* was prepared for the meeting. Also, *TERA* helped prepare the other toxicologists for the meeting by providing toxicity reports and summary information. The CATT toxicologists met on May 6 and 7, 2002 at EPA offices in Cincinnati, Ohio. The minutes of this meeting are provided in Section 2.2. The meeting lasted approximately 18 hours with roughly one-third of that time spent in discussions of C8's potential carcinogenicity. The oral provisional reference dose (pRfD) risk factor, and the two health protective SLs (for water and soil) based on this risk factor were developed at this meeting. The panel agreed that the toxicology database was insufficient to develop a dermal exposure pRfD. The inhalation provisional reference concentration (pRfC) risk factor and air SL developed at the meeting were only interim because additional data collection was necessary for their calculation. These data were collected and provided to *TERA*, who calculated the final pRfC and air SL, wrote a report describing this activity and forwarded it to the other CATT toxicologists for their approval. This document is provided in Section 2.3 as the post meeting action items. Both the meeting minutes and the post meeting action items were reviewed and approved by the panel of 10 highly qualified toxicologists.

An internal briefing for the DEP, DHHR, and EPA was held on May 8, 2002 to discuss the water and soil SLs. Rather than withhold this information while the meeting minutes report was prepared, DEP released the water and soil SLs so that the public would be informed of the status of their drinking water, and decisions could be made regarding the provision of alternative water supplies. In that spirit, DuPont and the public were informed – via a meeting with the above regulators and a press release, respectively - of the water and soil SLs on May 9, 2002.

A second public meeting was held at Blennerhassett Junior High School on May 15, 2002, to inform the public of the details of the SL development and of the groundwater C8 concentrations that had been detected at that point. Dr. Becker first spoke regarding environmental health risks in general. Dr. Staats described the process used by the CATT toxicologists to arrive at the water and soil SLs. Finally, David Watkins (DEP, GIST chairman) presented the C8 analytical data for private and public water sources. Slides of the presentations given at this meeting are provided in Attachment IIb.

2.0 DEVELOPMENT OF RISK FACTORS AND SCREENING LEVELS

TERA was assigned to prepare for, host and document the meeting of the CATT toxicologists during which the provisional C8 risk factors (pRfDs and pRfC) would be developed by the group. The activities undertaken by *TERA* to prepare for the meeting are presented in Section 2.1. The actual minutes of the meeting are provided in Section 2.2., and the tasks conducted by *TERA* to develop the final air SL after the meeting at the direction of the panel are described in Section 2.3.

2.1 Pre Meeting Action Items

TERA is a nonprofit [501(c)(3)] corporation dedicated to the best use of toxicity data for the development of risk values. This organization is very well known and respected in the toxicology arena for their professionalism, wealth of knowledge, experience, and unbiased approach to deriving risk factors. All the non-*TERA* toxicologists on the CATT, whether from government agencies or industry, were in unanimous support of including *TERA* in this project.

TERA was tasked with compiling and reviewing the available toxicological data for C8. A literature search and review of these data was in draft by EPA Headquarters, this document was provided to *TERA*. The 3M submittals to AR-226 were provided to *TERA* by DEP. These data grew from a total of seven compact discs to 10 during the time period of this project. The AR-226 continues to grow with 3M submittals currently. The index of the first seven discs are provided in Attachment Va. Additionally, DEP conducted a literature search of C8 toxicity data on the National Library of Medicine's Medline and Toxline databases in June 2001. The results of these searches were provided to *TERA* by DEP as well. Also, documents submitted to DEP from DuPont in response to the EPA Region 3 request for information was made available to *TERA* by DEP, first by mailing relevant toxicology documents identified by Dr. Staats, and then by physically delivering all these documents to their Cincinnati office for *TERA* to sort and identify those deemed relevant and necessary for their work. Therefore, little literature searching or data retrieval was required of *TERA*.

After reviewing the existing C8 toxicology data, *TERA* selected studies that would be suitable for derivation of risk factors for the oral, dermal, and inhalation route of exposure. A list of the potential key studies was prepared. An indepth review of these studies was then conducted, and the details of the studies were summarized in tabular format. Next, *TERA* prepared a condensed table of these studies including critical effects and exposure levels identified by *TERA*, and blank columns for the other criteria necessary in the risk factor development process, such as the uncertainty factors. The documents listed below were provided to the other CATT toxicologists approximately two or three weeks prior to the meeting. *TERA* also prepared tables of suggested uncertainty factors, risk factors, and resulting SLs to DEP. These documents were discussed with Dr. Staats but were not distributed to the other toxicologists prior to the meeting in an effort not to influence their decisions, and not to give the false impression that the decisions on risk factor development had already been made and that the panel's purpose was simply to review *TERA*'s work. Rather, *TERA*'s suggestions would be presented at the meeting as a starting point for panel discussions and the development of the risk factors and SLs would be done as a group. The pre-meeting documents provided to the rest of the panel by *TERA* and DEP are contained in Attachment III. Also in Attachment III is a more detailed description of the decisions and methodology used by *TERA* in suggested risk factor development.

2.2 CATT TOXICOLOGISTS MEETING MINUTES

Meeting of C8 Assessment of Toxicity Team (CATT) Toxicologists

May 6 and 7, 2002

Andrew W. Breidenbach Environmental Research Center, Cincinnati, Ohio

Attendees:

Voting Team Members

John Cicmanec, D.V.M., M.S., ACLAM, USEPA Office of Research and Development
Joan Dollarhide, M.S., M.T.S.C., J.D., Toxicology Excellence for Risk Assessment (*TERA*)
Michael Dourson, Ph.D., D.A.B.T., *TERA*
Gerald Kennedy, E. I. Du Pont de Nemours, Inc.
Andrew Maier, Ph.D., C.I.H., *TERA*
Samuel Rotenberg, Ph.D., USEPA Region 3
Jennifer Seed, Ph.D., USEPA Office of Pollution Prevention and Toxics (may abstain from voting)
Dee Ann Staats, Ph.D. (Chairperson), West Virginia Department Environmental Protection (DEP)
John Wheeler, Ph.D., D.A.B.T., Agency for Toxic Substances Disease Registry (ATSDR)
(representing West Virginia Department of Health and Human Resources [DHHR])
John Whysner, M.D., Ph.D., D.A.B.T. (consulting for DuPont)

Invited Guests

John Butenhoff, Ph.D., 3M Company (study director)
Jim Sferra, M.S., Ohio EPA (observer)

Note taker

Daniel Briggs, Ph.D., D.A.B.T., *TERA*

Introduction

The toxicologists on the C8 Assessment of Toxicity Team (CATT) met on May 6 and 7, 2002, to develop provisional reference doses (pRfDs) and screening levels (SLs) for ammonium perfluorooctanoate (C8) as specified in Consent Order GWR-2001-019 between the West Virginia Department of Environmental Protection, the West Virginia Department of Health and Human Resources, and E. I. Du Pont de Nemours & Co., (DuPont) dated November 14, 2001. These screening levels apply only to DuPont at their West Virginia facilities as specified in this consent order. Any use of these pRfDs or SLs for any other purpose or by any other regulatory agency is solely their choice and responsibility.

The meeting opened with Dr. Staats announcing that this meeting was being held pursuant to the above-cited consent order as part of an enforcement action and was therefore closed to the public. Dr. Staats noted that, except for Dr. Butenhoff and Mr. Sferra who were invited guests, the panelists were named as part of the consent order and were free to enter into discussions and vote on issues. It was noted that Dr. Seed could abstain from voting at any time. The rules for the meeting were set forth as follows:

- The panel would strive for unanimous consensus, but if such consensus could not be reached, then the majority of votes would rule.
- The panel was expected to be cooperative and courteous with each other.
- The risk factors and screening levels would be developed together as a group, rather than simply by reviewing the work and suggestions of *TERA*.
- Votes would be taken at each decision point. After panel discussion on each point, a motion would be made on the floor. The chair would then repeat the motion and verbally poll each panel member individually. The chair would always vote last in order to not influence the voting.

TERA recorded the official minutes for the meeting. However, the chair recorded supplemental notes, which were provided *TERA* to assist in the preparation of the final Meeting Minutes Report. It was noted that specific discussion comments or votes would not be attributed to panel members (i.e., no names would be used) in the meeting report in order to facilitate full and open discussion among the team. It was also noted that *TERA* would distribute a draft meeting report to the CATT panel for their review and incorporate panel comments as appropriate. Each panel member would be asked to sign a statement agreeing that the meeting report is an accurate representation of the discussion and conclusions of the CATT Team. The original signatures will remain on file with the DEP.

The sequence of discussion on Monday, May 6 was oral noncancer assessment; dermal noncancer assessment and on Tuesday, May 7 was cancer assessment; inhalation noncancer assessment; oral screening level; and interim inhalation screening levels. (Note that Dr. Seed left the meeting at 2:30 pm on Tuesday, May 7, 2002; she was present and joined in all discussions through the cancer assessment.) However, for clarity, the meeting report is organized according to noncancer (oral, dermal, inhalation) assessment, cancer assessment, and screening levels. Below, under each heading is a brief description of *TERA*'s opening comments, followed by the panel discussion, and then the outcome of the panel discussion.

Noncancer Assessment: Review of the Oral Studies

Prior to the meeting, *TERA* evaluated the available human and animal health effects studies for C8. (A list of the documents and studies included in *TERA*'s prior review is provided in the Attachments). *TERA* evaluated the pool of available studies to identify the key studies that could be selected by the CATT panel as the basis for the pRfD. In narrowing the list of available studies, the available data were evaluated weighing considerations such as observed effect levels, study duration and quality, and applicability to human health. The judgments were made in a manner consistent with hazard identification and dose-response assessment practices used in current U.S. EPA risk assessments. Studies were generally given greater consideration as potential principal studies if they were at least of subchronic duration; identified NOAEL/LOAEL boundaries on the low end of the range provided by all the data; and had robust design (e.g., diverse array of endpoints, sufficient number of animals). From the total pool of available studies, *TERA* developed detailed summary tables for each of the key

studies having potential for being selected as the principal study for derivation of the pRfD. The resulting detailed summary table of key studies was provided to the panel members prior to the meeting to facilitate the selection of the principal study by the CATT panel and is attached. Therefore, discussion of the oral studies at the meeting focused on the tables presented in the attachment which identified those studies of sufficient duration, content, and quality to merit consideration as the bases for deriving a pRfD. The tables present *TERA*'s selection of critical effect levels, and highlight the study data for key parameters that showed treatment-related changes.

At the opening of the meeting, the panel discussed whether all adequate studies had been included and whether any potential key studies were missing. One panelist asked why the 90-day Rhesus monkey study (Goldenthal, 1978b) had not been included. *TERA* responded that the Rhesus study was not considered to be as useful as the cynomolgus monkey study (Thomford et al., 2001) because it had fewer animals per group, and suggested a higher NOAEL/LOAEL boundary; however, findings from the Rhesus study would be discussed together with the cynomolgus study as supporting data. The panel confirmed that, to the best of their knowledge, the table included all of the toxicity work that should be considered in selecting principal studies for deriving the pRfD for C8.

After agreeing that all of the potential critical studies had been identified, the panel then discussed the merits of each of the studies, and the appropriate No-Observed-Adverse-Effect-Levels (NOAELs), Lowest-Observed-Adverse-Effect-Levels (LOAELs), and lower bounds on the benchmark doses (BMDLs) for each study.

Human Studies (Olsen et al. 2000; Olsen et al. 1998; Gilliland and Mandel 1996; Gilliland and Mandel 1993; Ubel et al. 1980)

TERA initiated the discussion by providing a brief synopsis on the potential utility of the available human health effects studies for deriving the pRfD. Two cohort mortality studies were available: (1) Ubel et al. (1980) reviewed the records of 180 deceased 3M employees for a period of 30 years (1948-1978) and found no significant difference between observed and expected mortality rates; (2) Gilliland and Mandel (1993) found no increases in mortality rates from liver cancer or liver disease in 3,537 (2,788 males and 749 females) exposed 3M workers for 35 years (1947 – 1983). Note that since the CATT meeting, a new epidemiological study on almost 4,000 (80% male) 3M workers has been completed which found no increase incidence of cancer in C8 exposed workers. Several cross-sectional studies of 3M workers (111, 80, and 74 males in 1993, 1995, and 1997, respectively) were available. However, these studies were noted as being limited for use in deriving the pRfD, since workers were exposed to unknown amounts of C8 for varying time periods, and no clear signs of toxicity (such as elevated serum levels of liver enzymes were reported). The mixed findings regarding changes in hormone levels were noted. It was noted that many of these studies provided data on serum levels of C8 (or serum fluorine levels), which could serve as a measure of exposure. However, the current toxicokinetics data were not viewed as sufficiently developed to conduct a quantitative extrapolation from the reported serum levels to equivalent oral doses in humans. Based on this introduction, the panelists were asked to comment on the human data and its usefulness for deriving the pRfD.

Key Panel Discussion Points: Panelists noted that, although limited, the existing human data are consistent with the animal data when exposure levels are considered. Although weaknesses in the epidemiology data were noted, one panel member commented that the human data are useful for hazard identification purposes, and provide some level of comfort in conducting the assessment since they do not identify adverse effects in chronically exposed workers. It was noted that a few of the

human subjects had C8 serum levels comparable to those observed in animal studies [20 parts per million (ppm) or greater]. Other panel members described gaps in the human studies. Regarding the absence of effects observed in the epidemiology studies, the panel noted that the small number of female subjects and uncertainties in exposure levels for workers prevents the existing data from being used to rule out human toxicity. For example, the very small numbers of women in the studies prevent drawing a conclusion regarding female reproductive effects. One panelist noted that the increased blood level of estradiol reported in some subjects is not clinically significant. In addition, no adjustments were made for body mass index (BMI) variations among subjects. Since BMI is known to affect estradiol levels and in this study BMI was the only parameter to correlate with hormone levels, it was noted that it is unlikely that C8 exposure was related to increased estradiol levels. The panel discussed Gilliland and Mandel (1986), which reported six prostate cancer deaths overall and four among exposed workers. One panel member commented on the update to this study (no study report was provided), which showed no indication of increased risk of prostate cancer. This follow up study demonstrated that only one of the four workers with prostrate cancer were determined to have been exposed when work history records and blood levels of C8 were examined.

It was suggested that it might be possible to correlate C8 serum concentrations with lack of observed toxicity to estimate a human NOAEL. However, it was noted that the lack of clear exposure levels in the human studies precluded this type of analysis. Although C8 half-life determinations were conducted in some of the human studies, this information cannot be used to determine exposure doses because some exposure to the subjects may still be occurring. However, it is clear that humans do not have the major sex-related half-life difference that exists in rats. It was noted that a physiologically-based pharmacokinetic (PBPK) model is being developed, which may be useful in estimating exposure concentrations from human serum C8 levels. However, a panel member familiar with the status of this current toxicokinetic modeling effort, noted that the data are not sufficiently developed to use for quantitative risk assessment purposes at this time.

Outcome: The panel agreed unanimously that the human studies were not adequate to be used for quantitative dose-response determinations. The human studies have many substantial data gaps, such as low numbers of subjects and unknown exposure concentrations. No LOAEL was established and the exposure uncertainty does not allow identification of a clear NOAEL. In final comments made during polling of the panel, one panel member agreed with the group, but noted that the data could be used to develop a bounding estimate. A second panel member added that some evidence suggests the endocrine system as a target for C8 effects, and therefore, the human data might support the animal toxicity studies.

Definition of Adverse Liver Effect

TERA noted that in all experimental animal studies liver effects occurred. For the purposes of conducting this assessment, *TERA* defined adverse liver effects as the presence of histopathology (moderate grade hypertrophy would be considered sufficient) in addition to statistically significant absolute or relative weight changes, or a liver weight change of 10% or greater. A doubling of serum levels of liver enzyme activity (e.g., alkaline phosphatase (ALP), aspartate aminotransferase (AST), or alanine aminotransferase (ALT)) would also indicate an adverse liver effect. These adverse effects are used by other health organizations as well. The panel unanimously agreed with this general definition of adverse for liver effects, but noted that individual studies could demonstrate a continuum of liver effects that could be considered biologically significant.

Palazzolo et al. 1993

This is a 90-day study in male rats in which animals received C8 at doses of 0, 0.05, 0.47, 1.44, and 4.97 mg/kg-day in feed. The major finding in this study was increased liver weight with histopathological findings such as moderate hypertrophy. Panelists were asked to comment on the data from this study; on the selection of study adverse effect levels; and on the usefulness of this study as the basis for deriving a pRfD.

Key Panel Discussion Points: The possible role of peroxisome proliferation in the observed liver effects was discussed. The panel discussed uncertainty in the relevance of this mechanism to humans. One panelist stated that when considering the relevance of peroxisome proliferation, it is important to consider both qualitative and quantitative issues. This panelist suggested that peroxisome proliferation may potentially occur in humans because the cellular receptor that modulates this reaction in rodents has been found in humans, but that this mode of action should be considered to be only qualitatively relevant to humans because the receptor is far less expressed in humans, and humans have not been shown to manifest a peroxisome proliferation response. It was noted that USEPA has an on-going project to investigate the relevance to humans of rodent peroxisome proliferation effects, but at this time EPA has no official policy on the significance of peroxisome proliferation for humans. It was also noted that IARC has also considered the issue of peroxisome proliferation and concluded that this mode of action is not relevant to humans if it has not been demonstrated to occur in human cells or primates treated with the chemical in question. (Note that the panel discussed the role of peroxisome proliferation as a potential mode of action for tumor formation later in the meeting. The results of this discussion are documented in the section on Cancer Mode of Action)

Discussion occurred regarding the usefulness of relative versus absolute liver weight in determining adverse effect levels. One panelist stated that changes in both of these parameters are preferred before designating a dose as an adverse effect level. However, most panelists considered a change in relative liver weight to be sufficient to designate a dose level as an adverse effect level. It was noted that liver weights in dosed animals in this study were comparable to control values after an 8-week recovery period; however, the panel agreed that this recovery should not influence selection of the NOAEL and LOAEL values.

Outcome: The panel agreed unanimously that 1.44 mg/kg-day is the LOAEL for this study because at this level statistically-significant increases in relative liver weight and CoA oxidase activity occur. In addition, hepatocellular hypertrophy of minimal severity or greater is observed in 14 of 15 animals at this dose, and in 2 of 15 animals at grade 2 or higher. The panel recommended that benchmark dose modeling be performed for the data based on grade 2 or higher hepatocyte hypertrophy. This modeling was conducted during the course of the meeting, resulting in a BMDL estimate of 1.3 mg/kg-day. It was noted that this BMDL is essentially the same as the LOAEL found in this study. Most panelists believed 0.47 mg/kg-day is the NOAEL because at this dose there are no statistically significant changes in either absolute or relative liver weight and only a "minimal" severity of hepatocellular hypertrophy is reported at this dose. However, one panel member preferred to call this a "minimal LOAEL" rather than a NOAEL, noting that dose-related changes in critical liver parameters had been established at the lower dose levels and suggesting that these could be part of the continuum of effects that might be considered a minimal LOAEL.

Goldenthal 1978a

This is a 90-day study in male and female rats in which animals received C8 in their feed at doses of 0, 0.56, 1.72, 5.64, 17.9, or 63.5 mg/kg-day for males and 0, 0.74, 2.3, 7.7, 22.4, or 76.5 mg/kg-day for females. This study is limited by the small number of animals (5/sex) in each dose group. Therefore, this study was not considered to be a key study. However, it was presented for the panel's consideration and comments because it includes female as well as male animals and the data on relative liver weights allow a BMD to be calculated.

Key Panel Discussion Points: One panelist noted that a sex difference was observed in this study. Another mentioned that this study demonstrates the importance of internal dose (C8 serum level), as compared to the administered dose.

Outcome: The panel agreed with the proposed NOAEL, LOAEL, and BMDL as presented by *TERA*. However, the panel also agreed unanimously that the study was not adequate to serve as the basis for deriving a pRfD because of limitations in the study (e.g., the small number of animals).

York 2002

This is a two-generation reproduction study in which male and female rats received C8 doses of 0, 1, 3, 10, and 30 mg/kg-day by gavage in distilled water. Parental animals were exposed through cohabitation and gestation to weaning of F1 animals, approximately 6 weeks. F1 animals were exposed from weaning until weaning of the F2 generation. The primary findings were increased liver weight and liver pathology in P and F1 generation male animals; however, it was noted that histology was conducted only when gross effects had been observed, and therefore liver histopathology data were not available for the control and low-dose F1 generation males.

Key Panel Discussion Points: One panelist stated that this was study was of excellent quality because it was conducted according to OPPTS guidelines for 2-generation studies. Two panelists noted that the degree of F1 generation exposure to C8 while *in utero* and while nursing was uncertain and may not have occurred at all because of rapid elimination of C8 from the systemic circulation of the female rats after it was administered via gavage. Therefore, the lack of reproductive toxicity in this study may not be meaningful. Other panelists agreed, but stated that the fact of rapid clearance resulting in decreased fetal exposure may not be relevant for humans because women do not have the same active secretory mechanism for C8 that exists in the female rat. Another panelist noted that rodent placenta provides less of an anatomical barrier than exists in primates. Another panelist observed that studies with radiolabeled C8 demonstrated that C8 could cross the placental barrier in rats. One panelist wondered whether female rat pups at weaning have developed the active secretory mechanism for C8 that exists in the mature females. Another panelist recalled data showing that weanling female rats were able to clear C8 faster than males, but not as fast as mature females. One panelist recommended that delayed sexual maturation and increased frequency of estrous cycles be included in the adverse effects noted for females for this study. A panelist pointed out that this study indicated a critical difference in the toxicity of C8 versus the structurally similar perfluorocarbon PFOS; in that PFOS caused fetal death at birth in a similarly designed study, while in this study C8 administration was associated with only a slightly statistically significant increase in fetal death at the post-weaning timeframe.

Outcome: The panel concluded that the LOAEL for males is 1 mg/kg-day. The males showed statistically-significant increases in liver and kidney weights at 1 mg/kg-day. No histology was conducted on liver and kidney at this dose level because no gross lesions were seen. However, given

the substantial histopathology noted at the next higher dose level (3 mg/kg-day), the panel believed pathology does exist at the 1 mg/kg-day level; therefore this level meets the agreed-upon definition of an adverse effect. The panel concluded that the LOAEL for females is 30 mg/kg-day. The females showed several adverse effects at this dose level, including increased mortality and decreased body weight. No NOAEL was identified for males; the NOAEL for females is 10 mg/kg-day. All of these values apply to both the P and F1 generation animals. Two panel members reviewed the BMDL modeling results, and agreed with the selection of 0.42 mg/kg-day as the study BMDL.

Riker Laboratories 1983

This is a chronic, 2-year study in male and female rats in which animals received C8 in feed at doses of 0, 1.3, and 14 mg/kg-day for males and 0, 1.6, and 16 mg/kg-day for females. The primary findings in this study are liver effects in male rats. However, it was noted that this chronic study also reported non-hepatic effects (ovarian stromal hyperplasia and ataxia) in female rats. Although this effect was not found in the subchronic study that included females (Goldenthal, 1978), the small number of animals in that subchronic study (n=5) may have limited the power of the study to observe these effects.

Key Panel Discussion Points: One of the panelists identified some copying errors in the tables (incidences of mammary fibroadenomas, Leydig cell adenomas, and ALT activity in the control group) and these values were corrected prior to the panel discussion (the attached table presents the corrected values). The panel disagreed with the study author's conclusion stated in the study report that the testicular vascular mineralization was a "spontaneous change occurring in aging rats" and that the ovarian stromal tubular hyperplasia was "equivocally related" to C8 administration because it did not progress. The panel considered both these effects to be biologically significant and relevant for determining adverse effect levels. One panelist stated that ovarian stromal hyperplasia is not commonly found in rats and noted that in this study the incidence of ovarian stromal hyperplasia in the control animals is zero. The panel discussed the relevance of the ataxia observed in females, but did not reach any conclusions about its possible biological significance. One panelist noted that at the time this study was conducted, the term "hepatic megalocytosis" was synonymous with the term "hepatic hypertrophy" currently in use. It was noted that the BMDL of 0.73 mg/kg-day calculated based on liver effects in males is consistent with the NOAELs for liver effects observed in other rat studies. In the initial summary table from which the panel was working it was noted that no BMDL was estimated for ovarian stromal tubular hyperplasia, since an adequate fit to the data was not achieved. One reviewer suggested that a model fit might be possible using log-transformed data, since the study results showed a clear log-related response curve. This approach was applied during the meeting, and resulted in a best estimate of the BMDL of 1.6 mg/kg/day.

Outcome: The panel agreed unanimously to the proposed NOAEL of 1.3 mg/kg-day for males, with a corresponding LOAEL of 14 mg/kg-day based on the following adverse effects: increased liver weight, hepatic cystoid degeneration, increased ALT enzyme activity, and testicular vascular mineralization. The panel agreed that the LOAEL in females was 1.6 mg/kg-day based on a statistically significant increase in the incidence of ovarian stromal tubular hyperplasia, and that this study did not identify a NOAEL for females. The panel further agreed that the estimated BMDL from this study is 0.73 mg/kg-day based on liver effects in males as the benchmark response.

Thomford et al., 2001

This is a 26-week study in cynomolgus monkeys, in which animals received C8 at doses of 0, 3, 10, or 30/20 mg/kg-day by gastric intubation of gelatin capsule. Gastric capsule intubation was chosen as the method of C8 administration to avoid emesis, which had occurred in the earlier Rhesus monkey study (Goldenthal et al., 1978b). Even so, several animals had problems tolerating the highest C8 dosing; as a result, the high dose was either reduced or in some cases, discontinued. Afterwards, time-weighted average doses were used to approximate the C8 dose given to the high-dose group. One animal died in the high dose group; primary findings included clinical signs and altered liver weight. *TERA* presented that altered liver weight was not considered an adverse finding.

Key Panel Discussion Points: At least two panelists believed that the degree of absolute liver weight increase (30%) noted at the 3 mg/kg-day dose should be sufficient to identify this dose as the LOAEL. Other panelists responded that this weight increase resulted from mitochondrial proliferation, and therefore was an adaptive response, not an adverse effect. They also pointed out that, unlike laboratory rodents, cynomolgus monkeys routinely exhibit large genetic variations. As a result, large differences in organ weights among these animals is relatively common and a 30% difference between groups – especially small groups, as in this study – is not necessarily biologically meaningful. Some panelists attempted to compare this study with the study conducted in Rhesus monkeys in order to help define the LOAEL, but this was not possible due to the uncertainty of dosing caused by the emesis that occurred in the Rhesus study. One panelist asked if the dosing technique (gastric intubation of the drug contained in gelatin capsules) might have contributed to a large range of C8 blood levels because of differences in capsule disintegration rates. Another panelist responded that this was unlikely because, while the data sometimes demonstrated large inter-animal variations in blood levels, the intra-animal variation over several dose administrations was small. It was noted that C8 serum levels were essentially the same in the low and mid-dose groups: 74, 80, and 120 μg/mL at 3, 10, and 30/20 mg/kg-day, respectively. The panel concluded that the similarities in serum C8 levels may explain the very similar effects observed between the 3 and 10 mg/kg-day dose groups. One panelist noted that protein-binding saturation was similar between the monkey and human.

Outcome: The panel agreed that the LOAEL is best described as "from 3 to 10 mg/kg-day" based on 30% increased absolute liver weight, and that a NOAEL does not exist for this study. At all three dose levels, statistically significant increases in absolute and relative liver weights occurred, but without accompanying histopathology. No clinical or histopathological evidence of organ damage occurred at any of the three dose levels. Dose-related trends toward lower T3 and T4 levels were observed, but these failed to achieve statistical significance, even at the highest dose. The panel concluded that these data are insufficient to identify any single dose as a LOAEL or NOAEL. Since the serum C8 levels were essentially the same for both the 3 and 10 mg/kg-day doses, the panel believed that designating a range of 3 to 10 mg/kg-day for the LOAEL is the best way to describe the study results.

Noncancer Assessment: Oral Hazard and Dose-Response Characterization

(Note: Dr. Seed abstained from voting during this part of the meeting.)

Critical Study and Point-of-Departure

The summary of NOAELs, LOAELs, and BMDLs unanimously agreed to by the panel is presented in Table 1 below. The individual study adverse effect levels were discussed by the panel for the purpose of selecting a critical study and effect level for derivation of the pRfD.

Key Panel Discussion Points: The primary target organ for C8 is the liver, and males are clearly more sensitive to this effect than female rats. One panelist observed that the liver effects in rats may be related to peroxisome proliferation, and therefore may not be quantitatively relevant for humans. For this reason, the liver effects in rats might not be an appropriate critical endpoint Another panelist responded that, because of this, it was important to note that the monkey and rat LOAELs are in the same range, and since the liver effects in monkeys may not be related to peroxisome proliferation, liver toxicity might also be a relevant endpoint for humans. The observation of ovarian effects in female rats at the same LOAEL as liver effects in males was noted as a second reason to consider the rodent studies as an appropriate basis for deriving the pRfD.

Table 1. Summary of NOAELs, LOAELs, BMDLs, and Critical Effects for Key and Supporting C8 Studies

	Species	Sex	NOAEL	LOAEL	BMDL	Critical Effect
Key Studies						
Palazzolo et al. (1993)	Rat	M	0.47	1.44	1.3	Liver
York et al. (2002)	Rat	M	None	1	0.42	Liver
Riker Laboratories (1983)	Rat	F	None	1.6	1.6	Ovary
		M	1.3	14	0.73	Liver
Thomford et al. (2001)	Monkey	M	None	3-10	None	Liver
Supporting Studies						
Goldenthal et al. (1987a)	Rat	M	0.56	1.72	0.44	Liver
Goldenthal et al. (1987b)	Monkey	M,F	3	10	Not done	Clinical signs

Some panelists favored choosing the monkey study as the critical study, due to the closer biological relationship with humans as opposed to rats. It was also noted that the observed increase in liver weight in monkeys may not be related to peroxisome proliferation and, therefore, may be more relevant for human health risk assessment. Other panelists disagreed, pointing to the uncertainties in dosing and effects, the small number of animals per dose group, and the unclear boundary between NOAEL and LOAEL values. Also, it was noted that the monkey study could not be considered the critical study because the 90-day, two-generation, and two-year rat studies all have LOAEL, NOAEL, and /or BMDLs below the LOAEL range identified in the monkey study, and therefore based on selection of the critical study with the lowest adequate NOAEL/LOAEL boundary would support the use of the rodent studies.

The panel considered whether it would be better to base the pRfD on a NOAEL or on a BMDL. Some panelists thought a NOAEL basis is a simpler concept and would be easier to explain to the public. Others responded that the BMDL captures more information from the entire study (e.g., reflects information from the full dose-response curve, and variability in the dose-response data) and therefore is the better choice as the basis for the quantitative dose-response assessment. Another panel member mentioned that a NOAEL is not a "no effect" level, rather it reflects the proportion of the responding population that can physically be observed in an experimental situation. Therefore, the size of the population is important. The panel agreed to not rule out using either a NOAEL or BMDL, but instead to focus on the quality of each study and the lowest critical effect level it provided.

The panel noted the unusually good agreement of the NOAELs and LOAELs from all the studies. The lowest NOAEL observed in one of the potential key studies was 0.47 mg/kg-day, from the 90-day rat study by Palazzolo et al. (1993). The lowest LOAEL observed in a key study was 1 mg/kg-day from the rat two-generation study (York et al., 2002). This study did not test doses low enough to identify a NOAEL; however, the BMDL value estimated for this study, 0.42 mg/kg-day, was essentially the same as the observed NOAEL from the 90-day study. Therefore, the panel agreed that the BMDL was an appropriate NOAEL surrogate for the two-generation study. The ovarian stromal hyperplasia reported in the chronic rat study (Riker Laboratories, 1983), provided a higher LOAEL than the two-generation study, and the BMDL for this effect resulted in the same value as the LOAEL. This demonstrates that the liver endpoint is the critical effect, because it occurs at lower doses.

Outcome: Because of the consistency in NOAELs/LOAELs and critical effect in all the key studies, the panel concluded that all studies could be considered co-critical studies and that all provide important information for human risk assessment. However, the panel unanimously agreed that the NOAEL surrogate from the two-generation study, a BMDL of 0.42 mg/kg-day, should serve as the point-of-departure for the pRfD. This value was selected since it represented the lowest NOAEL or BMDL, and provided the added consideration of having evaluated reproductive and developmental effects.

Uncertainty Factors

If adequate human data are available, these data are used as the basis for noncancer risk factor development. Otherwise, animal study data are used, along with a series of professional judgments that are incorporated into the risk factor as "Uncertainty Factors" and account for an assessment of the relevance and scientific quality of the experimental studies. There are five different uncertainty factors commonly used to address issues of biological variability and uncertainty. Two factors (Interspecies and Intraspecies) are used to address variability or heterogeneity that exists between animals and humans, and within different human populations. Three factors (Subchronic, LOAEL, Database) are used to address lack of information. Typically, the maximum total uncertainty factor that EPA will apply is 3000. If all five areas of uncertainty/variability are present warranting a total UF of 10,000, then EPA generally concludes that the uncertainty is too great to develop an RfD. The panel discussed each area of variability or uncertainty separately. A short introduction to each area of uncertainty is provided below to aid the reader in evaluating the discussions of the panel.

Intraspecies Variability (UF_H): This factor accounts for the natural differences that occur between human subpopulations and for the fact that some individuals may be more sensitive than the average population. This factor is composed of two subfactors – one to account for toxicokinetic differences (how the body distributes and metabolizes the chemical) and one to account for toxicodynamic differences (how the body responds to the chemical). If no information is available on human variability, then a default value of 10 is used. If adequate information is available on one of the two subcomponents, then this information is used along with a default value of 3 for the remaining subfactor. If data are available to adequately describe human variability in both subfactors, then actual data may be used to replace default values. In addition, if a RfD is based on human data gathered in the known sensitive subpopulation, a value of 1 may be chosen for this factor.

The panel discussed the lack of available data describing human variability. One panelist suggested a comparison of human C8 blood levels and values from the animal studies. The highest human serum C8 level reported was 111 ppm, but the average was approximately 5 ppm. No effects were noted in the human subject with the highest blood level. Thus, at least some people achieved serum C8 levels equivalent to those that resulted in adverse effects in animal studies.

As noted in the discussion of the human data above, the panel acknowledged gaps in the data on human variability and inability to define the most sensitive subpopulation, and therefore concluded that the default value of 10 was appropriate for this factor.

Interspecies Variability (UF_A): This factor accounts for the differences that occur between animals and humans and is also thought to be composed of subfactors for toxicokinetics and toxicodynamics. If no information is available on the quantitative differences between animals and humans, then a default value of 10 is used. If information is available on one of the two subcomponents, then this information is used along with a default value of 3 for the remaining subfactor. If data are available to adequately describe variability in both subfactors, then actual data may be used to replace default values. In addition, if a RfD is based on human data, then a value of 1 is appropriate for this factor.

One panelist mentioned that EPA has often used a UF_A value of 3 in other assessments when extrapolating monkey data to humans, because the kinetics and dynamics of monkeys are assumed to be similar to humans. This assumption is based on the fact that rhesus monkeys and macaques share a 92% genetic homology with humans and because monkey studies are able to detect a much broader range of clinical findings and more specific histopathology than rodents. In addition, studies on other chemicals in which a good database exists in rodents, monkeys and humans demonstrate that results in monkey studies parallel the human effects more closely than results in rodent studies.

Another panelist agreed and said the half-life of chemicals in monkeys was usually closer to humans than to rats. Other panelists responded that for C8, the half-life in monkeys is about 30 days; and this is much less than the C8 half-life in humans, which is estimated to be greater than one year. It was noted, however, that data on C8 half-life in humans is limited.

Because no data are available to warrant moving from the default, the panel unanimously agreed that a UF_A value of 10 is appropriate with either the rat or monkey toxicology studies.

Subchronic to Chronic Extrapolation (UF_S): Because the RfD protects for a lifetime exposure, this factor is applied when the database lacks information on the health effects of the chemical following a chronic exposure. Two issues are considered when making judgment on the use of this factor – are there data demonstrating that different health effects are expected following chronic exposure than subchronic exposure, and are there data demonstrating that the observed health effects progress in severity as exposure duration increases? If the database contains no information on chronic exposure, a default value of 10 is often applied, unless other data suggest a lack of progression with exposure duration. If the database contains adequate chronic bioassays, then a value of 1 is appropriate. If there are data addressing only one of the two issues, then a default of 3 may be applied.

It was noted that the database for C8 contains an adequate chronic rat study (Riker Laboratories, 1983). In addition, a second chronic study (Biegel et al., 2001) was available, although this study focused primarily on tumorigenic mechanisms in rats. In addition, for the purpose of evaluating uncertainty factors, the human occupational studies were considered by the panel to be informative on the response (or lack thereof) of humans following long-term exposure. The database demonstrates that liver

toxicity was the more sensitive endpoint in both subchronic and chronic studies. In addition, the database clearly demonstrates that liver toxicity does not progress in severity following chronic exposure. This conclusion is supported by the observation that the subchronic studies identified lower NOAELs for liver toxicity than the chronic studies. One panelist noted that the liver effect in rat progresses to cancer. However the panel concluded that the cancer effect was due to the peroxisome proliferation mechanism (as discussed below in the discussion of the cancer risk assessment). Based on these considerations, the panel unanimously agreed that a UF_S value of 1 is appropriate for the rat studies.

The panel also discussed whether a different value for UF_S would be appropriate if the monkey study had been used as the critical or co-critical study. One panelist observed that there were no data in monkeys regarding the progression beyond 26 weeks; another responded that there was no reason to think the effects in monkeys would be any more progressive than those in rats. Another panelist suggested that the toxicity of C8 in humans does not appear to be progressive. However, the panel agreed that there was some inherent uncertainty in the monkey study to justify use of the value of 3 for UF_S if the monkey study were the critical study.

LOAEL to NOAEL Extrapolation (UF_L): Because the RfD is considered to be a subthreshold value that protects against any adverse health effects, this factor is applied when the database lacks information to identify a NOAEL. If the database does not identify a NOAEL, then a default of 10 is used for this factor. If a NOAEL is used, a value of 1 is appropriate. Often, if the database does not identify a NOAEL, but the adverse effects observed are of minimal severity, then a default of 3 will be considered appropriate for use of a "minimal LOAEL". [1]

Several of the studies considered as co-critical identified NOAELs; the lowest NOAEL is 0.47 mg/kg-day from the 90-day study. Also, the BMDL estimated for the two-generation study was essentially the same as the observed NOAEL from the 90-day study. These NOAELs and BMDLs were based on well-conducted studies and their use as a basis of the pRfD is consistent with standard practice. Therefore, the panel had confidence that the C8 database has identified the threshold for toxicity in rats, and it unanimously agreed a UF_L value of 1 is appropriate for the critical effect in the rat studies.

The panel also considered the value of UF_L that would be appropriate if the monkey study were to be used as the critical study. Because there is no clear NOAEL value, the panel agreed that a value of 1 was not appropriate. However, because the effects seen at the low dose were limited to mild increases in liver weight without accompanying changes in histopathology, or any other effect, the low dose was considered to be a minimal LOAEL. Therefore, the panel agreed that a UF_L of 3 would be appropriate if the monkey study were to be used as the critical study.

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[1] EPA is currently discussing the application of UF_L when using a BMDL. A BMDL value represents the lower limit on the dose that should cause 10% of the experimental animals to respond with the effect that is being modeled. Because animal studies typically cannot detect a response less than 10%, an experimentally derived NOAEL also represents the dose that causes 10% of the animals to respond. For this reason, EPA has historically considered a BMDL to be a NOAEL surrogate and selected a UF_L value of 1 when a BMDL is used. Although EPA does not have official guidance on this issue, recent discussions in the agency suggest that if the effect being modeled for the BMDL is adverse, then the BMDL should be considered as a LOAEL. Currently, BMDLs are being evaluated on a case-by-case basis, considering the nature of the effect being modeled and the relationship of the estimated BMDL to observed NOAELs.

Database (UF_D): The database for deriving a high confidence RfD includes two chronic bioassays by the appropriate route of exposure in different species, one two-generation reproductive toxicity study, and two developmental toxicity studies in different species. The minimal database required for deriving a RfD is a single subchronic bioassay, that includes a full histopathology examination. The database factor is used to account for the fact that a potential health effect may not be identified if the database is missing a particular type of study. This factor may also be used if the existing data indicate the potential for a heath effect that is not fully characterized by the standard bioassays, for example neurotoxicity or immunotoxicity. If the database is complete, a value of 1 is appropriate. If only the minimal database is available, then a default of 10 is used. A value of 3 may be used if the database is missing one or two key studies.

The panel agreed that the oral database for C8 is complete. For the purpose of evaluating uncertainty factors, the panel felt that the human occupational studies provided sufficient information on the effects of long-term exposure in humans to function as a chronic bioassay. In addition, the consistency between the monkey and rat subchronic studies provides confidence that non-rodent species respond similarly to rats and that liver is a sensitive target organ in all species. Furthermore, a developmental toxicology study indicated that such effects only occurred at high concentrations, and reproductive effects were monitored in the 2-generation reproductive study.

Therefore, the panel unanimously concluded that a UF_D value of 1 is appropriate with either the rat or monkey toxicology studies selected as the critical study.

Outcome: The summary of the panel's unanimous conclusions regarding individual and composite uncertainty factors is presented in Table 2 below. The composite uncertainty factor is obtained by multiplying the individual factors. (Note, that following EPA convention, an uncertainty factor of 3 actually represents the log of the halfway point between 1 and 10. Therefore multiplying half-log values of 3 results in a full log value of 10, rather than 9 as would be expected for numeric multiplication.)

Table 2. Panel Recommendations of UF Selection for Oral pRfD

Study	UF_H	UF_A	UF_L	UF_D	UF_S	Composite UF
All Rat	10	10	1	1	1	100
Monkey	10	10	3	1	3	1000

Oral Reference Dose (RfD)

The final value of the RfD is obtained by dividing the point-of-departure by the composite uncertainty factor. As discussed above, the point-of-departure selected by the panel is the BMDL of 0.42 mg/kg-day estimated from the rat two-generation study (York et al., 2002) and the composite factor is 100. Therefore, the resulting pRfD is 0.42 ÷ 100, or 0.0042 mg/kg-day. Because of the lack of precision inherent in the RfD, only one significant figure is appropriate; therefore, this value is rounded to 0.004 mg/kg-day.

For comparison purposes, the panel considered the pRfD values that would result from choosing alternative NOAELs or BMDLs as the point of departure. This analysis is presented in Table 3 below:

Table 3. Comparison of pRfDs Derived Using Different Studies

Study	UF	NOAEL	RfD	BMDL	RfD
Palazzolo et al. (1993)	100	0.47	0.005	0.72	0.007
Riker Laboratories (1983)	100	1.3	0.01	0.73	0.007
York et al. (2002)	100	---	---	0.42	0.004
Thomford et al. (2001)	1000	3-10 (LOAEL)	0.003-0.01	---	---

Based on this review table developed by the panel, the pRfDs that could be derived from the C8 oral database range from 0.003 to 0.01 – at most a factor of 3 separates the different potential pRfDs. Considering that the definition of the RfD states that the RfD incorporates uncertainty spanning an order of magnitude (a 10-fold variation), the panel noted that close agreement of the potential pRfD values provides added confidence in the derived pRfD of 0.004 mg/kg-day.

Noncancer Assessment: Review of the Dermal Studies

(Note: Dr. Seed abstained from voting during this part of the meeting)

The data on C8 by the dermal route of exposure are limited. Other than acute lethality, skin sensitization, and irritation studies, the dermal database consists of only a single 2-week study.

Kennedy et al. 1985

This is a two-week study in male rats in which animals had C8 applied to the skin for 6 hours/day, 5 days/week at doses of 0, 4.2, 42, and 420 mg/kg-day. Although this is a short-term study, it is the only candidate for possible use in determining a reference dose for the dermal route of administration. The primary effects observed were increased liver weight and liver pathology. A panelist noted that the study design prevented animals from ingesting the dermally-applied material. Although the amount of material inhaled was considered to be low, some inhalation almost certainly occurred in the dosed animal because the control animals had detectable C8 blood levels. It was also noted that the consistency of the material applied to the animals varied among the dose groups, depending on the concentration of C8 in the material matrix. In all instances the amount of material on the skin was considerably thicker than a monolayer, and therefore, the applied doses might not reflect accurately the absorbed doses of C8 in this study.

Key Panel Discussion Points: One panelist stated that this study could provide potentially useful information because systemic effects are observed at dose levels below those which cause portal of entry effects (skin irritation). The panel discussed whether it would be appropriate to extrapolate the results of this study to longer durations in order to derive a dermal pRfD. The panel concluded that such extrapolation would not be advisable because of the possibility of unpredictable longer-term dermal effects. One panelist asked if route-to-route extrapolation could be done from the oral studies

to estimate a dermal NOAEL or LOAEL. Other panelists thought this would not be possible due to uncertainties in the C8 toxicokinetics by oral versus dermal exposure routes. For example, enterohepatic circulation is known to occur following oral exposure, but would not occur following dermal exposure. Therefore, the toxicokinetics of C8 is different between the two routes of exposure. Regardless of the route of entry, C8 is not metabolized. Furthermore, no data on the dermal absorption rate were identified. One panelist noted that if the findings from this study were used to determine a reference dose, the resulting value would be higher than the reference dose obtained from the oral studies. Therefore, using oral studies to set the reference dose would be adequately protective, of systemic exposure via the dermal route. Another panelist agreed, stating that no dermal reference dose should be identified at all, and that a specific reference dose for dermal exposure was not needed.

Outcome: The panel agreed unanimously that this study should not be used to determine a dermal pRfD because of uncertainties inherent in the study design as noted in the discussion.

Noncancer Assessment: Review of the Inhalation Studies

(Note: Dr. Seed was absent during this part of the meeting)

The data on C8 by the inhalation route of exposure are limited. Other than acute lethality studies, the inhalation database consists of a 2-week study and a developmental toxicity study.

Kennedy et al. 1986 and Staples et al. 1981

Two inhalation studies were discussed as potential candidates for deriving the pRfC. Kennedy et al. (1986) reported a two-week study in male rats in which animals were exposed head-only 6 hours/day, 5 days/week to C8 air concentrations of 0, 1, 7.6, or 84 mg/m^3. The primary effects observed in this study at the mid-concentration included increased absolute and relative liver weight, supported by clinical chemistry and histopathology findings. The high concentration resulted in severe toxicity, including mortality in one rat. Other findings at the high concentration group were increased lung and testes weight. A concentration-dependent increase in the incidence of nasal and ocular discharge was noted.

A second potential critical study for deriving the pRfC was a developmental toxicity study by Staples et al. (1981). Pregnant rats were exposed whole-body 6 hours/day on gestation days 6 to 15 to C8 air concentrations of 0, 0.14, 1.2, 9.9, and 21.0 mg/m^3.

The panel agreed the Kennedy two-week study provided the highest quality data for possible determination of critical effects and provided a slightly lower NOAEL/LOAEL boundary, even though both studies used similar air concentrations. In addition, the Kennedy et al. (1986) study evaluated a broader array of systemic endpoints, and included a histopathology examination.

In describing their initial review of the study, *TERA* noted that EPA's RfC methodology states that the air concentrations to which animals are exposed are to be converted to "Human Equivalent Concentrations ($Conc_{HEC}$)" by applying dosimetric adjustments (USEPA, 1994). Dosimetric adjustments account for the different structure and surface area of animal respiratory tracts compared with humans. Different dosimetric adjustments are applied depending on where effects are observed. For example, a different dosimetric adjustment will be applied for liver effects than will be applied for lung effects. *TERA* noted that the key piece of data needed to calculate the $Conc_{HEC}$ is a description of the particle size distribution (i.e., the mass median aerodynamic diameter and geometric standard

deviation or GSD). Data available from the published study did not provide complete information about the mass median aerodynamic diameter for the low-concentration group, or GSD for any exposure group. In order to facilitate the discussion of the study, *TERA* presented human equivalent concentrations for liver (extrarespiratory) and lung (pulmonary) effects from this study assuming either a monodisperse particle size distribution or a polydisperse particle size distribution. These results were presented to the panel as shown in Table 4 below.

Table 4. Preliminary $Conc_{HEC}$ Calculations from Kennedy et al. (1986)

Study Concentration[a]	GSD = 1.3 (Monodisperse)		GSD = 3 (Polydisperse)	
	Liver	Lung	Liver	Lung
1.0	0.6	0.018	0.5	0.09
7.6	4.6	0.14	4.0	0.70
84	67.7	17.7	46.9	7.4

a. All values are presented in units of mg/m^3.

Key Panel Discussion Points: It was noted that the inhalation database does not meet the minimum database requirements for determining an RfC of one subchronic 90-day study that includes histopathology of the respiratory tract, but that the consent order required a pRfC in order to set air screening levels. One panelist stated that it was not appropriate to extrapolate from oral studies to derive a RfC because of the absence of data on toxicokinetics differences between these routes (e.g., effects of enterohepatic circulation, or absorption).

One panel member indicated that the data needed to calculate the $Conc_{HEC}$ (i.e., the mass median aerodynamic diameter [MMAD] and geometric standard deviation [GSD]), but not reported, in the published study could be made available to *TERA* after the meeting. The panel agreed that these data should be provided to *TERA*, for calculation of the appropriate $Conc_{HEC}$ following the meeting. The panel then discussed whether the lung or the liver was the critical organ, recognizing that the final designation of critical effect could not be made until the correct $Conc_{HEC}$ is calculated. *TERA* raised the question of whether the reported increases in the incidence of nasal and ocular discharge should be considered an adverse effect. It was noted that this effect is not uncommon for the exposure protocol that was used, and the effect was seen in all groups. It was further noted that C8 is not an irritant, and that no nasal histopathology was observed in exposed animals. In selecting critical study concentrations the panel discussed the lung effects at higher doses. One panel member suggested that at the high concentration the overt pulmonary toxicity was observed due to the large particle burden. Uncertainties in interpreting the lung effects were raised by the panel. One panelist noted that the studies were too short to determine what effect chronic exposure would have on the respiratory tract. Another suggested that existing human data associated with the human study reports discussed earlier (pulmonary function testing of workers, etc.) might be useful in determining NOAEL/LOAEL values. After this discussion, the panel considered the study concentration of 7.6 mg/m^3 to be the NOAEL for pulmonary effects, with the LOAEL of 84 mg/m^3.

The panel next discussed the liver effects. It was noted that the observed increases in liver weight were consistent with the effects observed in the oral studies. Another panel member noted the increased alkaline phosphatase (AP) values observed at the higher doses were not necessarily the result of the types of liver effects seen in the oral and dermal studies, since increased AP levels often reflect disorders of biliary flow. One panelist questioned the ability of the study to detect systemic effects given the short exposure period and the kinetics of the compound; however, another panelist replied that the half-life of C8 in rats is 5 to 7 days, and the study design would have allowed achievement of

steady-state concentrations in the blood. The panel considered the study concentration of 1.0 mg/m^3 as the NOAEL for liver effects. However, one reviewer suggested that if the liver effects are found to be the critical effect based on the $Conc_{HEC}$, then benchmark concentration modeling should be conducted before assigning a critical effect level.

The panel considered the appropriate uncertainty factors for a pRfC, noting that the final choice of an appropriate value for some areas of uncertainty may change depending on whether lung or liver effects are found to be critical. (Note to the reader: Essentially the same areas of uncertainty are considered in developing a RfC as for the RfD. For a full explanation of the purpose for each factor, see the earlier discussion.) For the same reasons as discussed for the pRfD, the panel unanimously agreed that a value of 10 was appropriate for UF_H. When considering interspecies extrapolation, it is generally considered that the dosimetric adjustments used to derive the $Conc_{HEC}$ account for the toxicokinetic differences between animals and humans. Therefore, the uncertainty factor only needs to address the toxicodynamic differences. Since there are no data regarding dynamic differences between rats and humans, the panel agreed that the default value of 3 was appropriate for UF_A. Since the Kennedy study identified a NOAEL, the panel unanimously agreed that a value of 1 was appropriate for UF_L.

The panel considered that two of the factors, UF_S and UF_D, were related to the decision of whether lung or liver is the critical effect. If liver effects are determined to be the critical effect, then at least one panelist felt that UF_S, could be addressed with an uncertainty factor of 1 because the oral studies provided enough information to be confident that the liver effects would not progress in severity following a chronic inhalation exposure. However, other panel members stated that there were insufficient data to assess whether liver would continue to be the critical effect or to provide information on how the respiratory tract would respond following longer-term inhalation exposures, and that a value greater than 1 for UF_S was needed. For the UF_S and liver as the critical organ, the panel votes were 1, 3, or 10 with the majority choosing 3. If liver effects are determined to be the critical effect, then panelists were split on the value of the uncertainty factor for UF_D, choosing values of either 3 or 10 with the majority of the panel choosing 3. No unanimous consensus was reached on these two factors; however, a clear majority vote was reached on uncertainty factors of 3 each for UF_S and UF_D in reference to liver as the target organ.

If lung effects are determined to be critical, the panel was divided almost equally on the appropriate value for UF_S with opinions covering the full range of options from 1 to 3 to 10. Note however, that six scientists voted for a factor less than 10 (either 1 or 3) and five scientists voted for a value greater than 1 (3 or 10). Similarly, the panel was divided on the appropriate value for UF_D; panel opinions covered the full range of options from 1 to 3 to 10 with the majority of panelists choosing 3.

As noted above, after each discussion votes were taken on individual factors. These votes are shown in Table 5. Note that one scientist was reviewing the dosimetric adjustment calculations during this discussion and so was unable to vote on these UFs; also note that one more vote at any point in Table 5 would not have changed the final outcome. In addition, the panel did not reach consensus on the confidence in the RfC, with opinions ranging from "none" to "high" with the average being medium-to-low.

Table 5. Tally of Panel Votes for UF_S and UF_D						
	UF_S			UF_D		
Factor	1	3	10	1	3	10
Liver as critical	1	6	1	0	6	2
Lung as critical	3	3	2	1	5	2

Outcome: One panelist reminded the group that the purpose of Kennedy et al., (1986) was to identify the inhalation hazard, not to look closely at NOAEL, LOAEL, etc. A prospective inhalation study designed to look more closely at the NOAEL/LOAEL aspects, to evaluate lesions as a function of exposure time, and to evaluate tissues of the respiratory tract using up-to-date methodology would be valuable and would allow a more focused evaluation of the RfC. Nonetheless, the panel agreed that a pRfC could be developed, but this agreement was not unanimous. The panel also recommended that *TERA* obtain additional data on the particle size GSD value to determine the $Conc_{HEC}$ corresponding to the NOAEL before determining whether the pulmonary or the hepatic effects are considered critical. If the liver effects are determined to be the critical effect, then BMD modeling should be done. The composite uncertainty factor was expressed as a range of 30 to 3,000. The final pRfC is presented in the Post Meeting Action Items.

Cancer Assessment

(Note: Dr. Seed abstained from voting during this part of the meeting)

U.S. EPA's 1999 Guidelines for Carcinogen Risk Assessment were used to frame the discussion of C8 carcinogenic potential. *TERA* opened the discussion with a short introduction to these guidelines, highlighting the recent focus on evaluation of the mode of action data in developing a weight of evidence characterization, and in deciding the most appropriate dose-response approach, linear or margin of exposure (MOE). It was noted that the EPA's 1999 guidelines would be used as the basis for the deliberations of the panel.

Cancer Hazard Identification and Mode of Action

The panel discussed the evidence for C8 carcinogenicity in humans and agreed that the human carcinogenicity evidence is inconclusive. Although four prostate tumors were reported in retired workers, three of these four cases now are known to have had minimal or no C8 exposure. (See Human Studies section for more detailed discussion.)

The panel noted that two animal carcinogenicity studies had been conducted. The first study (Riker Laboratories, 1983) reported treatment-related increases in Leydig cell adenomas and mammary gland fibroadenomas. The second study (Biegel et al., 2001) reported treatment-related increases in tumors in the liver, Leydig cells, and pancreas. Panelists noted that the tumors identified in the Biegel et al. (2001) study correspond to the triad of tumors associated with some chemicals that cause peroxisome proliferation. Other panelists agreed and suggested that a further examination of the data may indicate that this triad of tumors can be best addressed using a MOE approach. The panel also noted that the mammary fibroadenomas may require the default linear model because, following U.S. EPA cancer guidelines, no actual mode of action data for C8 and this tumor type are available to warrant moving from the default assumption. Each of the four types of tumors found in the two C8 animal

carcinogenicity studies was then discussed in detail with regard to the weight of the evidence for the mode of action, and the evidence supporting a linear or MOE dose-response assessment approach. Listed below are the outcomes and discussions for each tumor type.

Liver tumors

Key Panel Discussion Points: The discussion on liver tumors focused on the role of peroxisome proliferation as the mode of action for the observed liver tumors. In relating this liver tumor effect to humans, one panelist said humans are much less sensitive to peroxisome proliferation than rats. Another panelist noted that IARC's approach for clofibrate and other non-genotoxic peroxisome proliferation chemicals was to assume that the mode of action was not relevant to humans if no evidence of peroxisome proliferation was observed in humans. Another panelist said that although rats may be more sensitive than humans from a toxicodynamic standpoint (due to interspecies differences in receptors), humans may be more sensitive from a toxicokinetic standpoint, since they clear C8 more slowly than rats. As a result, the panel member suggested that these two considerations would tend to decrease overall differences in species sensitivity. On the other hand, a panel member noted that no increased incidence of tumors have been found in people taking clofibrate, a known peroxisome proliferator, which suggests that humans are much less sensitive to peroxisome proliferation than rats and they may have no response at all. Based on these data, the panel member suggested that the lack of tumor development in humans exposed to C8 should not be discounted. The panel discussed differences in results between the two cancer studies. One panelist noted the studies have differences in their internal delivered doses because of differences in the animal diets. This could explain the difference noted in toxic effects.

Outcome: The majority of the panel agreed that the data indicate peroxisome proliferation is the mode of action for the liver tumors, and that although the liver tumor response is not likely to be quantitatively similar between rats and humans, the use of the liver tumor response data for human health risk assessment cannot be totally discounted. However, other scientists indicated that based on the lack of peroxisome proliferation in the non-human primate studies, the rodent liver tumors are not relevant at all to humans.

Leydig Cell Tumors

Key Panel Discussion Points: In reviewing the summary tables prepared for the meeting, one panelist noted that Leydig cell hyperplasia should be evaluated. In response, the hyperplasia data from Biegel et al. (2001) was reviewed by the panel. The panel developed Table 6 to facilitate the comparison on hyperplasia and tumorigenic outcomes.

Table 6. Summary of Beigel et al., 2001 Leydig Cell Data

	Pair fed controls	300 ppm
Liver carcinomas/adenomas	3/79	10/76*
Leydig ademonas	2/78	8/76*
Pancreatic carcinomas/adenomas	1/79	8/76*
Leydig cell hyperplasia	26/78	35/76

The panel noted that no significant increase in Leydig cell hyperplasia was apparent from these data; however, due to different survival times between the two groups (C8 treated animals survived longer) a false positive effect could have occurred because older animals would have more time to develop naturally occurring tumors. It was noted that a more formal analysis would be needed to determine whether the incidence of Leydig cell tumors would still be increased after adjusting for differences in survival, but the formal statistical analysis was too complex to complete during the meeting.

The panel discussed the role of peroxisome proliferation as the mode of action of Leydig cell tumors. Specifically, the panel discussed a workshop publication (Clegg et al. 1997) that evaluated the seven known modes of action for Leydig cell tumors. Most of the modes of action involve altered hormonal response in response to peroxisome proliferation, including increased estradiol via hepatic aromatase and binding to the TGF α receptor or elevations in leutinizing hormone to compensate for the testes becoming less responsive to this hormone. One panelist emphasized that the monkey study (Thomford et al., 2001) showed no effects in the testes, even though the animals were dosed at C8 levels high enough to cause major weight loss and mortality. This panelist suggested that this indicates the Leydig cell effects seen in rats are unlikely to occur in primates. This panel member also noted that no increased estradiol was noted in the monkeys.

One panelist observed that Leydig cell tumors were a classic response to peroxisome proliferation but the available studies do not provide positive evidence, such as increased estradiol levels, that peroxisome proliferation is the operative mode of action. The panelists agreed that while data gaps exist, a peroxisome proliferation mode of action was a reasonable assumption. One panelist stated that whatever the MOA was, it was not genotoxicity.

The panel agreed unanimously that for Leydig cell tumors:

- All 7 possible mechanisms for Leydig cell tumors are non-linear; therefore a non-linear dose-response approach is reasonable;
- Humans have a low incidence of these tumors;
- The monkey study did not demonstrate Leydig cell pathology or increased estradiol;
- Leydig cell tumors are a known tumor type for other peroxisome proliferators;
- Humans do not develop Leydig cell tumors following exposure to other known peroxisome proliferators such as clofibrate;
- Regardless of the actual mode of action, it is likely to be non-genotoxic.

Outcome: The panel agreed that based on the absence of genotoxicity, the Leydig cell tumors were likely to be caused by a non-genotoxic mechanism. The panel further agreed that if sufficient evidence were available to show increased estradiol levels (i.e., secondary to peroxisome proliferation) as the mechanism for the observed tumors, then the mechanism would be non-genotoxic and would not be quantitatively similar or possibly not relevant at all to humans. However, without this evidence this effect can not be totally discounted.

Pancreatic tumors

Key Panel Discussion Points: Since the tumor results from the Beigel et al., (2001) were not provided in the summary table distributed to the panel prior to the meeting, the pancreatic tumor data from this study were presented as a table at the meeting (see Table 7 below):

Table 7 Biegel Study: Pancreas Tumors			
	Control	pair-fed control	300 ppm
Hyperplasia	14/80 (18%)	8/79 (10%)	30/48* (40%)
Adenomas	0/80	1/79	7/76*
Carcinomas	0/80	0/79	1/76

One panelist described an analysis that had been done to compare the two cancer studies with regard to the pancreatic tumors. This panelist noted that although the first study (Riker Laboratories, 1983) did not report pancreatic tumors or hyperplasia, the second study (Biegel et al., 2001) did. However, this panel member also noted that the studies were not inconsistent because of the different definitions of adenoma versus hyperplasia based on pancreatic cell size used by the respective investigators. Also, the criteria for separating hyperplasia from adenomas is based on lesion size. Both studies were qualitatively similar with a number of larger lesions (adenomas) found in the Biegel study. Another scientist commented, when the two studies were recently compared by a group of pathologists using current criteria, there was a consistency in a pancreatic response; however, there was not an increased number of adenomas found in the earlier study. Instead, an increase in hyperplastic nodules of the acinar pancreas was found, which is consistent with the Beigel study. However, even though the dietary dose was the same (300 ppm), the Riker Laboratories study rats did not develop these hyperplasias into adenomas to the extent that occurred in the Beigel study.

With regard to the potential mode of action, one panelist suggested that the persistent increase seen in cholecystokinin and increased bile acids may be involved in the MOA, but the evidence in rats, monkeys and humans does not support this hypothesis. When a panelist asked if a strong case could be made that the pancreatic tumors resulted from peroxisome proliferation, several panelists responded no. Another added that while some peroxisome proliferation agents cause the triad of tumors seen with C8, not all do. Another panelist added that no pancreatic, liver, or testes hyperplasia was noted in monkeys at the time of sacrifice.

Outcome: The panel agreed that the evidence was not sufficient to demonstrate the MOA for pancreatic tumors, but enhanced cell proliferation (hyperplasia) was likely to be involved. The MOA appears to be non-genotoxic based on the results of genotoxicity bioassays.

Mammary Fibroadenomas

Key Panel Discussion Points: The panel considered whether the fibroadenomas observed in the Riker Laboratories study were a real treatment-related effect, or an artifact of classification, since other mammary tumor types observed in this study showed no clear relationship with dose. Table 8 below shows the data for several types of mammary tumors from this study:

Table 8. Riker Study: Mammary Tumors

	Control	30 PPM	300 PPM
Adenomas	7%	0	0
Adenocarcinomas	15%	31%	11%
Carcinomas	2%	0	0
Fibroadenomas	22%	42%	48%*

One panelist suggested that even though fibroadenomas were statistically significant, when all mammary tumor types are combined, they are not likely to be significant. It was noted by the panel that the individual incidence data from the study would need to be examined to determine the combined incidence of all mammary tumor types, rather than adding the percentages from each category. The panel discussed the histological basis for reporting separately fibroadenomas versus other types of mammary adenomas. A panelist suggested that since fibroadenomas do not progress to the other types it is correct to report them separately. Another said that the National Toxicology Program (NTP) reports fibroadenomas combined with adenomas.

The panel also discussed potential modes of action for mammary tumors. Increased estradiol was proposed as a possible MOA for the induction of hyperplasia and tumor formation, but the panel did not believe the data were sufficient to demonstrate this proposed mode of action. A panelist asked if a linear assessment could be done to help decide the importance of the effect. Another responded that the data were not adequately fit by any of the acceptable dose-response models, so a quantitative dose-response assessment was not reported for this data set.

Outcome: The panel agreed the data are not adequate to demonstrate a MOA; however based on the negative genotoxicity assays, C8 is unlikely to be genotoxic. Several panelists were not convinced the data demonstrated any real tumorigenic effect.

Cancer Dose-Response Assessment

After evaluating the relevance of each tumor type to humans, and the potential mode of action, the panel members were asked to recommend a dose-response approach for each tumor type. In all cases the panel agreed unanimously unless noted otherwise. For the liver tumors, the panel agreed that the MOE approach was most appropriate. For the remaining tumor types, the panel agreed that both linear and MOE approaches were appropriate, since the mode of action was not considered to have been adequately demonstrated for any of these three tumor types. All panel members agreed with these conclusions, except for the Leydig cell tumors, where one panel member argued that only an MOE approach should be used.

For the liver tumors, the MOE approach was selected. Since the MOE analysis often uses the benchmark response for a precursor as the basis of deriving a point of departure, the panel judged the pRfD for liver effects as sufficiently protective of potential liver carcinogenicity.

For Leydig cell tumors, benchmark dose modeling was conducted to identify a point of departure for the linear and MOE assessments. The Point of Departure (POD) for Leydig cell was chosen by the panel from the BMD modeling output. The BMDL of 0.32 mg/kg-day was selected as the most appropriate basis for deriving the assessment.

The panel discussed the appropriate factors to apply to the BMR for completing the MOE assessment. The panel noted that EPA's 1999 guidelines have only recently begun to be applied, and that formal guidance or examples of the interpretation and default values to use in deriving the MOE are lacking. In discussing the important considerations for the MOE, the panel decided that the critical factors to be considered were for "Nature of Effect", Intrahuman sensitivity" and "Animal to Human Extrapolation". A summary of the factors chosen is shown in Table 9.

For the Leydig cell tumors, a factor of 3 for nature of effect was selected as the most appropriate value, since the observed effect was for benign tumors. A factor of 10 was selected for Intrahuman sensitivity. A factor of 3 was used for Animal to Human Extrapolation, since dosimetric adjustments were applied to the dose data used for the BMD modeling. This composite factor of 100 was further supported since these types of tumors, although common in rats, are found rarely in people. In addition, the mode of action is likely via peroxisome proliferation which is quantitatively much less important in humans. The panel agreed that the composite MOE of 100 was appropriate.

For the linear dose-response assessment for Leydig cell tumors the BMDL of 0.32 mg/kg-day was used to calculate an oral cancer slope factor as follows:

Slope factor = risk/dose = 0.1/0.32 = 0.31 per mg/kg-day

(Note: risk is numerically expressed as 0.1 because the BMDL is the point that represents a 10% increased in tumor incidence in accordance with EPA guidance.) BMD modeling failed for the tumor data for pancreatic tumors and mammary gland fibroadenomas. Therefore, the panel determined that the data for these two tumor types were not adequate to conduct a quantitative dose-response assessment.

Table 9.
Factors Used to Describe Various Areas in the Development of MOEs for Cancer Endpoints.

Tumor	Model	Nature Of Effect	Intra Human	Animal to Human	Steepness of Slope	Total Exposure	MOE
Liver	MOE	1	10	10	NR	NR	100
Leydig	both	3	10	3	NR	NR	100
Pancreas	both	NA (cannot be modeled)					
Mammary	both	NA (cannot be modeled)					

NR = Not Relevant based on panel judgment; NA = Not Applicable

The panel also voted on confidence ratings for the cancer assessment. *TERA* noted that according to EPA guidance "high confidence" suggests that the assessment is unlikely to change with the availability of new data, while "low confidence" indicates that the assessment is likely to change with new data. Based on these criteria the panel voted on their confidence in the cancer assessment using either the pRfD for liver toxicity to adequately account for the liver cancer risk or using the assessment based on Leydig cell tumors. The panel voted as follows:

Liver pRfD = high (7 votes); medium-high (2 votes)
Leydig tumors = low (7 votes); low-medium (2 votes)

Therefore, the panel agreed that the oral pRfD for liver toxicity would be the basis for determining water and soil screening levels (which are based primarily on oral exposure) for the following reasons:

- high confidence in the pRfD (i.e., not likely to change in the future due to additional data collection);
- the pRfD would be protective against the quantitatively less sensitive and questionable relevance peroxisome proliferation-related liver cancer in humans;
- low confidence in the Leydig tumor analysis and questionable relevance to humans;
- limitations in study design, data quality, and data interpretation rendered difficult the determination of whether the reported increased incidence of pancreatic tumors or mammary tumors were related to C8 treatment, and did not allow the modeling of a point of departure that could serve as the quantitative basis for risk value development.

Screening Levels

(Note: Dr. Seed was absent during this part of the meeting)

The consent order required that screening levels be developed for drinking water, soil, and air. The panel followed the guidance provided by U.S. EPA's "Risk Assessment Guidance for Superfund" as further explained by both Region 3 and Region 9 risk-based concentration guidance. In cases where a conflict occurred between the guidance documents, Region 9 guidance was followed because it is more conservative, i.e. more health protective. For drinking water and soil, only ingestion and dermal absorption were considered as routes of exposure. EPA guidance indicates volatilization from water or soil should only be evaluated for chemicals with Henry's law constants greater than 10^{-5} and molecular weights less than 200. Since C8's Henry's Law constant is 10^{-11} and its molecular weight is 431, volatilization was not evaluated.

As discussed above, the panel concluded that since both liver and Leydig cell tumors were potentially formed via nonlinear modes of action, and further since greater confidence was placed in the quantitative assessment based on the liver endpoint, the pRfD and pRfC for liver toxicity would be protective of potential cancer effects of C8. The panel considered that the linear extrapolation for Leydig cell tumors was too uncertain to be used with confidence and that the MOE approach based on the Leydig cell tumors gave essentially the same numerical value as that for the liver endpoint, but with less confidence. Thus, the pRfD and pRfC for liver toxicity, and "noncancer" equations were used for calculating screening levels. Screening levels are calculated following the premise that if lifetime exposure is equal to or less than the pRfD or pRfC, then no risk of deleterious effects is expected. Mathematically, this concept can be expressed by the following standard equation; the ratio of the measured or estimated exposure to the RfD is called the Hazard Quotient.

If Exposure ÷ RfD = 1 or less, then no risk of deleterious effects is presumed.

Using this concept, it is possible to estimate the concentration in media that results in a lifetime exposure equal to the pRfD or pRfC. These equations, from EPA Region 9's guidance on deriving risk based concentrations, are listed below:

Air Screening Level : $[\ ]\ ug/m^3 = \frac{THQ \times RfDi \times BW \times AT \times 1000}{EF \times ED \times \text{air IR}}$

Note: $RfDi\ (mg/kg\text{-}day) = RfC \times \frac{20 m^3/d\ (IR)}{70\ kg\ (BW)}$

Soil Screening Level: $[\ ]\ mg/kg = \frac{THQ \times AT \times BW}{EF \times ED \times [\text{soil IR} / RfD \times 10^{-6} + SA \times AF \times ABS / RfD \times 10^{-6}]}$

Water Screening Level: $[\ ]\ ug/L = \frac{THQ \times AT \times BW \times 1000}{EF \times ED \times [\text{water IR} / RfD]}$

Where:

THQ	=	Target Hazard Quotient, assumed to be 1
RfDi	=	The RfC expressed in terms of dose, mg/kg-day
RfD	=	The oral reference dose estimated by the panel, 0.004 mg/kg-day
RfC	=	The inhalation reference concentration estimated by the panel, see below
BW	=	Body weight, assumed to be 70 kg for adults and 15 kg for children
AT	=	Averaging time, 10950 days, the exposure duration expressed in days
EF	=	Exposure Frequency, 350 days/year, the average number of days each year people are exposed
ED	=	Exposure duration, 30 years, the average number of years people are exposed
IR	=	Inhalation rate for air screening levels, 20 m^3/day; Ingestion rate for soil and, Water screening levels, 200 mg/day soil ingested based on child exposure and, 2 L/day water ingested based on adult exposure
SA	=	Surface area of exposed skin, 2800 cm^2/day
AF	=	Adherence factor, 0.2 mg/cm^2, the amount of soil that adheres to skin
ABS	=	Skin absorption factor, specific factor not available for C8, assumed to be 0.1 for semi-volatile chemical per EPA guidance

The panel unanimously agreed that the equations, assumptions, and default exposure parameters described above were the appropriate choices for calculating screening levels for air, soil, and water. The following values are the screening levels estimated by the equations.

For air: 0.1–6.0 micrograms per cubic meter of air ($\mu g/m^3$) ambient air. Note that the panel considered this range to be interim until the additional work discussed for the RfC is completed. This range incorporates the range of possible $NOAEL_{HEC}$s estimated by *TERA* prior to the meeting as well as the range of composite uncertainty factors recommended by the panel. The final pRfC is discussed in the following section Post Meeting Action Items.

For soil: 244 miligrams per kilogram of soil (mg/kg) residential soil, rounded to 240 mg/kg.

For water: 146 micrograms per liter of water (µg/L), rounded to 150 µg/L.

2.3 POST MEETING ACTION ITEMS

The following activities were conducted after the CATT Toxicologists meeting.

Derivation of the pRfC for C8

The CATT panel could not develop a final recommendation on the pRfC or the air screening level during the May 6 and May 7, 2002 meeting. This was due to a lack of data necessary for these calculations. At the meeting, the panel chose the key study for risk factor derivation as the 2-week inhalation study by Kennedy et al. (1986) and voted upon the uncertainty factors. They directed the author, panel member Kennedy (DuPont), to (1) retrieve the standard deviation data for the absolute and relative liver weight data sets; and (2) to measure the particle size distribution in the exposure chamber and determine the corresponding standard deviation; and (3) to provide these data to DEP and to *TERA*. The panel directed *TERA* to utilize these data to develop the pRfC based on the most sensitive organ (liver or lung) and the air screening level based on USEPA Region 9 standard formulas.

During the meeting, the CATT panel agreed that the Kennedy et al. (1986) study was the most appropriate basis for deriving the pRfC, with the developmental study by Staples et al. (1981) providing support for the selected critical effect levels. The CATT panel identified a NOAEL for increased liver weight at the lowest study concentration of 1.0 mg/m^3, with a LOAEL of 7.6 mg/m^3. The NOAEL for lung effects was identified by the CATT panel as 7.6 mg/m^3, with a LOAEL was 84 mg/m^3.

In order to derive an pRfC, the reported study concentrations were converted to human equivalent concentrations ($Conc_{HEC}$), according to current U.S. EPA RfC methodology (USEPA, 1994). The calculation of the $Conc_{HEC}$ requires two steps. First, the study concentration is adjusted from the exposure duration used in the experiment to an equivalent continuous exposure concentration ($Conc_{ADJ}$). Animals in this study were dosed for 6 hours per day, for five days, then not dosed for two days, and dosed again for five days and sacrificed at the end of the 12th day; hence, continuous exposure duration adjustment was made as follows:

$$\text{Study concentration} \times (6 \text{ hours}/24 \text{ hours}) \times (10 \text{ days}/12 \text{ days}) = Conc_{ADJ}$$

Second, the duration-adjusted concentrations ($Conc_{ADJ}$) were converted to human equivalent concentrations ($Conc_{HEC}$) to account for differences in the respiratory tract anatomy and physiology for the test species versus humans. This conversion is made as follows:

$$Conc_{ADJ} \times RDDR = Conc_{HEC}$$

The RDDR is the Regional Dose Deposition Ratio calculated using U.S. EPA's RDDR software program (USEPA, 1994). The RDDR depends on the characteristics of the particle size distribution (e.g., mass median aerodynamic diameter, and geometric standard deviation), the test species and body weight, and the region of the respiratory tract (or extrarespiratory tissue target if applicable) affected by exposure. Appropriate particle size characteristics to use as inputs into the RDDR software were obtained from a recent communication from DuPont (see attached). For the Kennedy et al. (1986) study, the test sex and species was male rats. Since body weight data were provided in the study, these data were used directly in the RDDR program. The mean body weight data on day 5 of exposure was used for this calculation, rather than the study-day 10 body weight data. The day 5 body weights were

used because there was evidence of changes in body weight over the 12-day study period, and therefore, this value was judged as the best estimate of the mean body weight over the period of exposure.

The CATT panel considered two potential critical effects for deriving the pRfC; increased liver weight and overt toxicity secondary to pulmonary toxicity. The RDDR for extrarespiratory tissues was the most appropriate value to use in calculating human equivalent concentrations for assessing the liver effects. The RDDR program calculates values for a variety of different regions of the respiratory tract. The CATT panel agreed that the overt toxicity of C8 was likely due to particle overload, as supported by pulmonary edema in the acute study reported in the same paper (Kennedy et al., 1986). Therefore, the RDDR for the pulmonary region was selected as most appropriate respiratory tract region for calculating the human equivalent concentrations. The calculation of the human equivalent concentrations used in the dose-response assessment is summarized in Table 10.

Table 10. Calculation of Human Equivalent Concentrations for Kennedy et al. (1986)

		Extrarespiratory		Pulmonary	
Study Concentration[a]	$Conc_{ADJ}$	RDDR[b]	$Conc_{HEC}$	RDDR	$Conc_{HEC}$
1.0	0.21	2.956	0.62	0.513	0.11
7.6	1.6	2.954	4.7	0.512	0.81
84	17	2.973	52	0.521	9.1

a. All concentrations reported in the table are in units of mg/m^3.

b. The RDDR values are taken from the EPA RDDR Program Output provided in the attachment

Benchmark Concentration Modeling

The CATT panel further recommended that benchmark concentration (BMC) modeling be performed for the increased liver weight endpoint from the Kennedy et al. (1986) study. The published version of the study did not provide standard deviations to accompany the group mean data, and therefore, BMC modeling could not be performed at the time of the CATT panel meeting. Subsequent to the meeting, the individual liver weight data for this study were obtained from DuPont (see attached). The individual animal data were used to calculate group mean and standard deviations. These data were then employed for the BMC analyses.

The modeling was conducted according to draft EPA guidelines (U.S. EPA, 2000) using Benchmark Dose Software (BMDS version 1.3.1), available from the U.S. EPA website (U.S. EPA, 2002). The endpoints of interest with respect to C8 liver toxicity were continuous rather than quantal (e.g., incidence data) in nature. Therefore the absolute and relative liver weight data sets were modeled using the linear, Hill, power, and polynomial models. An acceptable fit to the data was defined as a goodness-of-fit p-value greater than or equal to 0.1, or a perfect fit when there were no degrees of freedom for a formal statistical test of fit. Choice of 0.1 is consistent with current U.S. EPA guidance for BMD modeling (U.S. EPA, 2000). Goodness-of-fit statistics are not designed to compare different models, particularly if the different models have different numbers of parameters. Within a family of models, adding parameters generally improves the fit. BMDS reports the Akaike Information Criterion (AIC) to aid in comparing the fit of different models. When comparing the fit of two or more

models to a single data set, the model with the lesser AIC was considered to provide a superior fit. The benchmark response (BMR) level used for this analysis was set at a standard deviation (SD) value of 1.0. This value was chosen based on EPA draft guidelines for BMC analysis (U.S. EPA, 2000), in the absence of a clear biological rationale for selecting an alternative response level.

The following guidance was followed with regard to the choice of the Benchmark Concentration Lower Limit (BMCL) to use as a point of departure for calculation of the pRfC. This guidance is consistent with recommendations in U.S. EPA's BMC guidance (2000). For each endpoint, the following procedure is recommended:

1. Models with an unacceptable fit are excluded.

2. If the BMCL values for the remaining models for a given endpoint are within a factor of 3, no model dependence is assumed, and the models are considered indistinguishable in the context of the precision of the methods. The models are then ranked according to the AIC, and the model with the lowest AIC is chosen as the basis for the BMCL.

3. If the BMCL values are not within a factor of 3, some model dependence is assumed, and the lowest BMCL is selected as a reasonable conservative estimate, unless it is an outlier compared to the results from all of the other models. Note that when outliers are removed, the remaining BMCLs may then be within a factor of 3, and so the criteria given in item 2 would be applied.

4. The BMCL values from all modeled endpoints are compared, along with any NOAELs or LOAELs from data sets that were not amenable to modeling, and the lowest NOAEL or BMCL is chosen.

The BMC results are summarized in Table 11 and the individual BMDS model run output is provided in the attachments.

For modeling of the absolute liver weight data set, a constant variance model was appropriate (see test 2 in the BMDS output). The power and polynomial models both defaulted to a linear model. None of these linear models fit the data well. The Hill model provided an excellent fit to the data, as indicated by visual inspection of the fit and the comparison of the maximum likelihood estimates for the fitted model to the optimum model (shown as model A1 in the BMDS output). The linear models failed to provide an adequate fit to the full data set, since they did not accommodate the plateau of the concentration-response curve between the mid- and high-concentrations. BMC modeling was redone using a truncated data set (high concentration group removed) to optimize the fits of these models. Removing the high concentration resulted in good fits for the linear models (the power and polynomial models again defaulted to linear) as indicated by the AIC and goodness-of-fit p-values. The Hill model could not be run with the truncated data set since at least four concentration groups are required to provide a model fit.

Adequate fits to the data were achieved when the high concentration data were removed. An argument could be made for using these results as the best estimate for the data set, since an adequate fit was achieved with fewer parameters than for the Hill model using the full data set. However, the BMCL estimate for the full data set was on the border of 3-fold lower than for the truncated data set, which would suggest that the lower BMCL should be selected. Furthermore, comparison of the chi square residuals in the range of the NOAEL concentration suggests that the Hill model provided a better fit of the data in the low concentration region than the linear models using the truncated data. Finally, since

there was no biological rationale for removing the high concentration data from the modeling, an adequate model fit for the full data set is preferred over the model fit for the truncated data set. Based on these considerations, the BMC of 0.78 mg/m^3 and corresponding BMCL of 0.33 mg/m^3 are considered the best estimates for the absolute liver weight data set.

The relative liver weight data displayed a similar plateau between the mid- and high-concentration groups. The linear, power, and polynomial models all failed to provide an adequate fit. As for the absolute liver weight data, the Hill model provided an excellent fit to the data, but in this case failed to calculate a BMCL. In the absence of an adequate BMCL estimate for any of the models using the full data set, the data were remodeled with the high concentration group data removed. The power and polynomial models were nearly linear, as indicated by the parameter estimates in the BMDS output. The linear, power, and polynomial models all provided a similar, and very good visual fit to the data. The goodness-of-fit statistic for the linear model was 0.9. Although BMDS did not calculate the goodness-of-fit p-values for the power and polynomial models, inspection of the maximum likelihood estimates for these fitted models as compared to the optimum model (model A1 in the BMDS output) confirmed the good fit. The linear model provided a similar BMC and BMCL estimate as the power and polynomial models, but required less parameters to do so (i.e., as reflected in the lower AIC). Therefore, the BMC of 1.3 mg/m^3 and the corresponding BMCL of 0.94 mg/m^3 are considered the best estimates for the data set for relative liver weight.

At the time of the meeting the CATT panel did not provide a recommendation on whether absolute or relative liver weight should be considered more appropriate as the critical effect. Both of these measures were significantly increased beginning in the 7.6 mg/m^3 study concentration group. One would not expect a difference in the sensitivity of these two measures in this case, because there was no change in body weight (the basis for calculating relative liver weight) at the NOAEL. Therefore, both absolute and relative liver weight changes are considered to be an adequate basis for the critical effect. Based on this consideration, the lower of the BMCL estimates for the absolute and relative liver weight changes is the most appropriate basis for deriving the pRfC. The BMC of 0.78 mg/m^3 with the corresponding BMCL of 0.33 mg/m^3 for increased absolute liver weight are the best estimates from the BMC modeling results. The BMCL of 0.33 mg/m^3 is the most appropriate choice as the critical effect level for derivation of the pRfC, because the BMCL is lower than either the NOAEL of 0.61 mg/m^3 for liver effects or the NOAEL of 0.81 mg/m^3 for pulmonary effects in this study.

Selection of uncertainty factors

As described in the technical meeting notes, the CATT panel unanimously agreed on the choice of 3 for extrapolation from an animal study (UF_A), a factor of 10 to account for variability in human sensitivity (UF_H), and a factor of 1 for extrapolation from study NOAEL or BMDL (UF_L). The CATT panel considered the selection of U.S. EPA's other two factors, for extrapolation from a study of less-than-lifetime duration (UF_S) and for database insufficiencies (UF_D), to be dependent on whether liver or lung was ultimately selected as the critical effect. The panel was not unanimous in selection of the UFs or UF_D for either organ, but a clear majority vote was obtained for these UFs regarding liver toxicity.

Based on the liver as a critical effect, panel members recommended values of either 1 (one vote), 3 (six votes) or 10 (1 vote) for UF_S, and values of 3 (six votes) or 10 (two votes) for UF_D. Therefore, based on the liver as the critical effect, the composite UF would range from 100 to 1000, depending on the selection of the values for UF_S and UF_D. The majority vote of the CATT panel (Table 5) supported a factor of 3 for UF_S and 3 for UF_D. Based on these values, a composite UF of 300 for liver effects was calculated.

Based on the lung as the critical effect, panel members recommended values of either 1(three votes), 3 (three votes) or 10 (two votes) for UF_S, and values of 1 (one vote), 3 (five votes), and 10 (two votes) for UF_D. Therefore, with the lung as the critical effect the composite UF would range from 30 to 3000. The majority of the CATT panel supported a value of 3 for UF_D based on lung effects. A clear majority vote was not determined for any one value for the UF_S; however, six votes were cast for a value lower than 10 and five votes were cast for a value higher than one; thus the median value of 3 would be a reasonable choice. Therefore, values of 3 for both UF_D and UF_S for lung effects would also result in a composite UF of 300.

However, it is important to note that the panel could not arrive at a consensus on the overall magnitudes of UF_S and UF_D, because of the numerous uncertainties with the inhalation database. The resulting range in the uncertainty factor was generally considered reasonable by the panel, with values falling within this range being indistinguishable from each other.

Calculation of the pRfC

Liver toxicity was identified as the critical effect because it was more sensitive to C8 than the lung (i.e., liver toxicity had a lower NOAEL or BMCL than lung), the composite UF ranged from 100 to 1000 and was 300 based on the majority vote.

The pRfC is calculated as follows:

$$\text{pRfC } (mg/m^3) = \text{critical effect level / composite UF}$$

$$\text{pRfC range} = 0.33 / 1000 = 0.00033 \text{ mg/m}^3 \text{ (or rounded to 0.3 } \mu g/m^3)$$
$$\text{to}$$
$$= 0.33 / 100 = 0.0033 \text{ mg/m}^3 \text{ (or rounded 3.3 } \mu g/m^3)$$

$$\text{pRfC (majority vote)} = 0.33 / 300 = 0.0011 \text{ mg/m}^3 \text{ (or rounded to 1 } \mu g/m^3)$$

Therefore, the recommended pRfC based on the majority vote for a composite UF of 300 is 1 microgram per cubic meter of air ($\mu g/m^3$) with a range from 0.3 $\mu g/m^3$ to 3.3 $\mu g/m^3$.

Table 11. Benchmark Dose Modeling Results for C8[a]				
Model/Data Set	**AIC**	**P-value**	**BMC[b]**	**BMCL**
Absolute Liver Weight –All Data Modeled				
Linear	62.58[c]	<0.001[d]	31	19
Hill	48.67	1.0[e]	**0.78**	**0.33**
Power	62.58[c]	<0.001	31	19
Polynomial	62.58[c]	<0.001	31	19
Absolute Liver Weight - High Concentration not Modeled				
Linear	38.22[c]	0.72	1.6	1.1
Power	38.22[c]	0.29[d]	1.6	1.1
Polynomial	38.22[c]	0.72	1.6	1.1
Hill	Insufficient Number of data points to run model			
Relative Liver Weight – All Data Modeled				
Linear	-167.65[c]	<0.001	21	15
Hill	-184.29	1.0[e]	1.1	Failed
Power	-167.65[c]	<0.001	21	15
Polynomial	-167.65[c]	<0.001	21	15
Relative Liver Weight - High Concentration not Modeled				
Linear	-137.04[c]	0.90	**1.3**	**0.94**
Power	-135.05[c]	Failed	1.5	0.94
Polynomial	-135.05[c]	1.0[e]	1.5	0.94
Hill	Insufficient Number of data points to run model			

[a] Modeling was performed based on absolute and relative liver weight results reported in Kennedy et al. (1986).

[b] BMC and BMCL are based on benchmark response of 1SD. Results are presented in units of mg/m^3. BMC and BMCL estimates in bold type are the estimates judged to be the best estimates for each endpoint. "Failed" indicates that BMDS was unable to produce the estimate or the information required to be able to present a value.

[c] Corrected from erroneous BMDS output. Errors were identified in the degrees of freedom (DF) provided in the output for the fitted model in several cases. For these cases, the AIC was calculated independently using the log likelihoods provided in the output and the correct number of DF. Similarly, the goodness-of-fit p-values were corrected by calculating manually the chi square p-value using the appropriate number of DF.

[d] This model provided an identical fit to the linear and polynomial models. The reported P-value reflects a difference in the maximum likelihood estimate for the comparison model (Model A1 in the BMDS output) across the three models. This difference the maximum likelihood estimate should be the same for all three models, since this estimate is model independent.

[e] A fit that maximizes the likelihood is assigned a p-value of 1.0, even if there were no degrees of freedom for a formal statistical test. The maximized likelihood is given by model A1 for constant variance models and model A2 for non-constant variance models. Models A1 and A2 are independent of the model chosen to fit the data (e.g., power, polynomial, Hill model) and provide the best match possible to the mean and standard deviation for each dose level.

Calculation of an Air Screening Level

As described in the technical meeting notes, U.S. EPA Region 9 methodology was judged by the CATT panel to be an appropriate basis for deriving the air screening level. The following standard formula was used to calculate the air screening level:

$$\text{Air Screening Level } (\mu g/m^3) = \frac{THQ \times RfDi \times BW \times AT \times 1000}{EF \times ED \times \text{air IR}}$$

$$\text{Note: } RfDi \text{ (mg/kg-day)} = RfC \times \frac{20 m^3/d \text{ (IR)}}{70 \text{ kg (BW)}}$$

Where:

THQ	=	Target Hazard Quotient, assumed to be 1
RfDi	=	The RfC expressed in terms of dose, mg/kg-day
RfC	=	The inhalation reference concentration (mg/m^3)
BW	=	Body weight, assumed to be 70 kg for adults
AT	=	Averaging time, 10,950 days, the exposure duration expressed in days
EF	=	Exposure Frequency, 350 days/year, the average number of days each year people are exposed
ED	=	Exposure duration, 30 years, the average number of years people are exposed
IR	=	Inhalation rate for air screening levels, 20 m^3/day

Using this equation, the air screening level ranges from 0.3 $\mu g/m^3$ to 10 $\mu g/m^3$. Using a reasonable median value, the air screening level would be 1.1 $\mu g/m^3$ (or rounded to 1 $\mu g/m^3$).

2.4 SUMMARY OF FINDINGS

The key studies, critical effects and levels, uncertainty factors, and provisional risk factors developed by the CATT toxicologists are summarized in Table 12.

Table 12. Summary of RfD and RfC Values for C8 Determined by the CATT Toxicologists									
Reference	**Critical Effect**	**Critical Effect Level[a]**	**UF_A**	**UF_H**	**UF_L**	**UF_S**	**UF_D**	**Composite UF[b]**	**RfD/RfC**
Oral Studies									
Palazzolo et al. (1993)[c] 90-day rat study	Increased relative liver weight with histopathology in male rats	0.47 (NOAEL in males) 0.72 (BMDL)	10	10	1	1	1	100	0.005 0.007
York et al. (2002) Two-Generation rat study	Increased liver weight in male rats, supported by histopathology at higher doses (histopathology was not examined at the lowest dose, but incidence of hypertrophy was 100% at next highest dose).	0.42 (BMDL in males)[d]	10	10	1	1	1	100	0.004
RikerLaboratories (1983) Two-year rat study	Hepatic megalocytosis in male rats.	0.73 (BMDL in males)	10	10	1	1	1	100	0.007
Thomford et al. (2001)[e]26-week cynomolgus monkey study	Decreased thyroid hormone levels in male cynomolgus monkeys, and supported by a NOAEL at the same dose for clinical signs of toxicity in the co-critical rhesus monkey study (Goldenthal et al., 1978b)	3 - 10 (LOAEL in males)	10	10	3	3	1	1000	0.003 - 0.01

Inhalation Studies									
Kennedy et al. (1986)[f] Two-week rat study	Increased liver weight supported by histopathology and clinical chemistry in male rats	0.61(NOAEL - HEC_{ex}males) 0.33 (BMCL, BMC 0.78 absolute liver weight) 0.94(BMCL, BMC 1.3 relative liver weight)	3	10	1	3	3	300	1
Dermal Studies									
Kennedy et al. (1985)[f] Two-week rat study	Increased liver weight in male rats	4.2[g] (LOAEL in males)							Data Inadequate

a. Oral and Dermal effect levels and RfDs are presented in units of mg/kg-day, while the inhalation critical effect level and RfC is presented in units of mg/m^3

b. Areas of uncertainty addressed by uncertainty factors are: animal to human extrapolation (A); intrahuman variability and protection of sensitive subpopulations (H); extrapolation from a LOAEL to a NOAEL(L); extrapolation from a subchronic to chronic exposure (S); and lack of a complete database (D)

c. The subchronic study by Goldenthal et al. (1978a) could serve as a supporting study for liver effects in rats.

d. BMDL is the 95% lower confidence limit on the dose corresponding to a response level of 10% or an increase of 1SD in the continuous endpoint being assessed. Only modeling results that provided the lowest value and provided an adequate fit to the data are provided.

e. The subchronic study in rhesus monkeys by Goldenthal et al. (1978b) is a co-critical study for clinical signs of toxicity in monkeys.

f. These studies are not adequate for derivation of an IRIS quality RfD/RfC of even low confidence. The values shown could be used to derive a provisional value. Derivation of the RfC or RfD via route-to-route extrapolation is not supported by the available toxicokinetic data. Consensus on the values for UF_s and UF_D was not reached by the panel; however, a majority vote was obtained for a value of 3 for both these UFs in reference to liver as the target organ. See text of this report for ranges of UFs and SLs based on the range distribution of the votes for UFs.

g. 4.2 mg/kg-day reflects the study dose of 20 mg/kg adjusted for discontinuous exposure.

I agree that the notes as presented accurately reflect the panel's discussion and conclusions during the May 6-7, 2002 C8 Assessment of Toxicity Toxicologists Panel Meeting, and that the post meeting actions taken to develop the pRfC and Air Screening Level are in accordance with the instructions provided to *TERA* by the panel. (Original signatures are on file at DEP.)

_____ _____

John Cicmanec, D.V.M., M.S., ACLAM, USEPA ORD Date

_____ _____

Joan Dollarhide, M.S., M.T.S.C., J.D., *TERA* Date

_____ _____

Michael Dourson, Ph.D., D.A.B.T., *TERA* Date

_____ _____

Gerald Kennedy, DuPont Date

_____ _____

Andrew Maier, Ph.D., C.I.H., *TERA* Date

_____ _____

Samuel Rotenberg, Ph.D., USEPA Region 3 Date

_____ _____

Jennifer Seed, Ph.D., USEPA Headquarters OPPT Date

_____ _____

Dee Ann Staats, Ph.D., DEP (Chairperson) Date

_____ _____

John Wheeler, Ph.D., D.A.B.T., ATSDR Date

_____ _____

John Whysner, M.D., Ph.D., D.A.B.T. Date

3. 0 COMPARISON OF SCREENING LEVELS TO SITE-RELATED DATA

After the SLs for air, water, and soil were determined, DEP compared these SLs to the site-related data that has been collected to date. These comparisons are summarized below. The work of the CATT was only one facet of an investigation that continues beyond the issuance of this report. The GIST is expected to issue a report of the groundwater and surface water data in early 2003. The air modeling effort continues and is currently focusing on determining the results of the air emissions reduction efforts by DuPont required in the consent order as a 50% reduction in overall emissions (both air and water) by the end of 2003. Upgrades were completed in June 2002 which included the installation of a new scrubber and increased height of the primary C8 emissions stack.

Water

To date, of the 188 samples collected from private wells, cisterns, and springs, 50 were used for drinking water and none exceeded the150 ppb health protective water SL for C8. Also to date, nine public water supply facilities in West Virginia have been analyzed for C8, including Belleville Locks and Dam, Blennerhassett Island, General Electric, Lubeck Public Service District (PSD), Mason County PSD, Parkersburg PSD, Racine Locks and Dam, New Haven Water Department, and Ravenswood. None of the drinking water from these facilities contained concentrations of C8 that exceeded the 150 ppb water SL. In fact, the concentrations of C8 in public water supplies were all below 2 ppb, below 15 ppb in private non-drinking water, and below 3 ppb in private drinking water wells in West Virginia. Samples were collected from Ohio public and private water supplies. Although C8 levels in some Ohio private water supplies were higher than those detected in West Virginia, none of these samples contained C8 concentrations above the water SL. These data have been provided to Ohio EPA and DEP will continue to share information with throughout the remainder of this investigation. The DEP notes that the water SL is higher than DuPont's internal community exposure guidelines for drinking water of 1 or 3 ppb; however, these guidelines were developed in the early 1990s and based solely on a two-week inhalation study from 1986. Since then significant additional toxicological data have been collected and the CATT water SL is based on a comprehensive examination of all available information. Sampling of the Ohio River has begun; preliminary analytical results are expected from the laboratory in September 2002. To date, no analysis has been performed to measure C8 in soils in West Virginia on private property; therefore, no comparison can be made to the soil SL.

Air

Mathematical computer models that incorporate weather conditions, chemical characteristics, and facility measurements were utilized by DEP to simulate the ambient air concentrations of C8. Based on actual emissions data from the DuPont WW facility for the year 2000, the DEP modeling efforts predicted a maximum C8 concentration in air of approximately 2.7 $\mu g/m^3$ at the facility fence line along the Ohio River. The maximum modeled C8 air concentration in the West Virginia residential area adjacent to the facility was approximately 0.2 $\mu g/m^3$ annual average. Predicted C8 air concentrations across the Ohio River from the WW facility in Ohio residential areas were greater than those predicted in residential areas in West Virginia. These data have been provided to Ohio EPA and DEP will continue to share information with Ohio EPA throughout the remainder of this investigation. Results of similar subsequent air modeling efforts conducted by DuPont are consistent with those of the DEP. Air modeling information can be obtained from the DEP Division of Air Quality.

The DEP's Divisions of Water Resources and Air Quality are currently reviewing all relevant air and water data to determine DuPont's compliance with the November 2001 consent order between DEP and DuPont.